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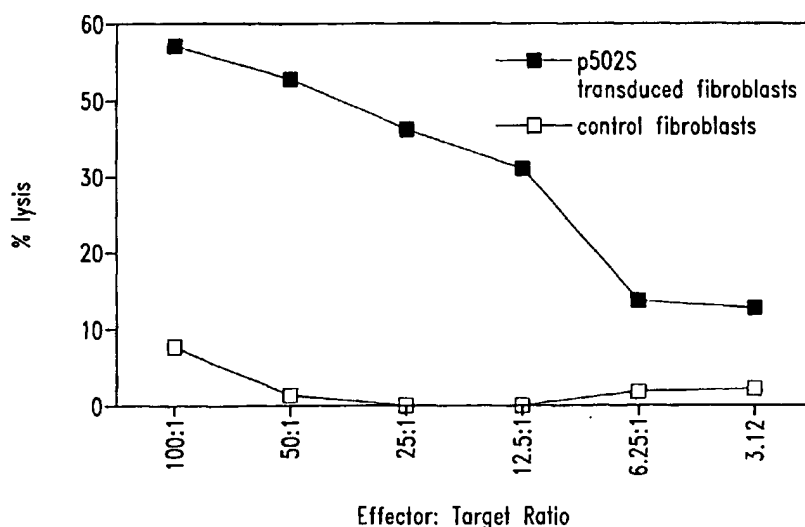
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[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER



(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate-specific proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate-specific protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate-specific protein, or mRNA encoding such a protein, in a sample are also provided.



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ning of each regular issue of the PCT Gazette.

COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER

5 TECHNICAL FIELD

The present invention relates generally to therapy and diagnosis of cancer, such as prostate cancer. The invention is more specifically related to polypeptides comprising at least a portion of a prostate-specific protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for
10 prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers.

BACKGROUND OF THE INVENTION

Prostate cancer is the most common form of cancer among males, with an estimated incidence of 30% in men over the age of 50. Overwhelming clinical evidence shows that human prostate cancer has the propensity to metastasize to bone, and the disease appears to progress
15 inevitably from androgen dependent to androgen refractory status, leading to increased patient mortality. This prevalent disease is currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate cancer remains difficult to treat. Commonly, treatment is based on surgery and/or radiation therapy, but
20 these methods are ineffective in a significant percentage of cases. Two previously identified prostate specific proteins - prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic potential. For example, PSA levels do not always correlate well with the presence of prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate
25 with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

30 SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the

diagnosis and therapy of cancer, such as prostate cancer. In one aspect, the present invention provides polypeptides comprising at least a portion of a prostate-specific protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536; (b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and (c) complements of any of the sequence of (a) or (b). In certain specific embodiments, such a polypeptide comprises at least a portion, or variant thereof, of a protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-550.

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a prostate-specific protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines for prophylactic or therapeutic use are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and an immunostimulant.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a prostate-specific protein; and (b) a physiologically acceptable carrier. In certain embodiments, the present invention provides monoclonal antibodies that specifically bind to an amino acid sequence selected from the group consisting of SEQ ID NO: 496, 504, 505, 509-517, 522 and 541-550, together with monoclonal antibodies comprising a complementarity determining region selected from the group consisting of SEQ ID NO: 502, 503 and 506-508.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

5 Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

10 Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an immunostimulant.

15 Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate-specific protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

20 Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

25 Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a prostate-specific protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be prostate cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain

embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that
5 hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b)
10 detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as
15 monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed
20 herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate-specific polypeptide P502S, as compared to control fibroblasts. The
25 percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate-specific polypeptide P502S. In each case, the number of γ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure
30 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/neu.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

5 Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse
10 Jurkat A2Kb cells expressing the representative prostate-specific polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

Figures 6A and 6B are graphs illustrating the specificity of a CD8⁺ cell line (3A-1) for a representative prostate-specific antigen (P501S). Figure 6A shows the results of a ⁵¹Cr release
15 assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target ratios as indicated.

Figure 7 is a Western blot showing the expression of P501S in baculovirus.

Figure 8 illustrates the results of epitope mapping studies on P501S.

20 Figure 9 is a schematic representation of the P501S protein showing the location of transmembrane domains and predicted intracellular and extracellular domains.

Figure 10 is a genomic map showing the location of the prostate genes P775P, P704P, B305D, P712P and P774P within the Cat Eye Syndrome region of chromosome 22q11.2

Figure 11 shows the results of an ELISA assay of antibody specificity to P501S
25 peptides.

SEQ ID NO: 1 is the determined cDNA sequence for F1-13

SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12

SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16

30 SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1

SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9

SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4

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SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12
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SEQ ID NO: 31 is the determined 3' cDNA sequence for J1-16
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SEQ ID NO: 35 is the determined 3' cDNA sequence for L1-2
SEQ ID NO: 36 is the determined 3' cDNA sequence for L1-6
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SEQ ID NO: 38 is the determined 3' cDNA sequence for N1-1860
SEQ ID NO: 39 is the determined 3' cDNA sequence for N1-1861

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SEQ ID NO: 106 is the determined cDNA sequence for 1D-4280

SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12 (also referred to as P504S)

5

SEQ ID NO: 108 is the predicted amino acid sequence for F1-12

SEQ ID NO: 109 is the determined full length cDNA sequence for J1-17

SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12 (also referred to as P501S)

SEQ ID NO: 111 is the determined full length cDNA sequence for N1-1862 (also referred to as

10 P503S)

SEQ ID NO: 112 is the predicted amino acid sequence for J1-17

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SEQ ID NO: 114 is the predicted amino acid sequence for N1-1862 (also referred to as P503S)

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- SEQ ID NO: 201 is the determined extended cDNA sequence for 1D.1-4278
- 5 SEQ ID NO: 202 is the determined extended cDNA sequence for 1D-4288
- SEQ ID NO: 203 is the determined extended cDNA sequence for 1D-4283
- SEQ ID NO: 204 is the determined extended cDNA sequence for 1D-4304
- SEQ ID NO: 205 is the determined extended cDNA sequence for 1D-4296
- SEQ ID NO: 206 is the determined extended cDNA sequence for 1D-4280
- 10 SEQ ID NO: 207 is the determined cDNA sequence for 10-d8fwd
- SEQ ID NO: 208 is the determined cDNA sequence for 10-H10con
- SEQ ID NO: 209 is the determined cDNA sequence for 11-C8rev
- SEQ ID NO: 210 is the determined cDNA sequence for 7.g6fwd
- SEQ ID NO: 211 is the determined cDNA sequence for 7.g6rev
- 15 SEQ ID NO: 212 is the determined cDNA sequence for 8-b5fwd
- SEQ ID NO: 213 is the determined cDNA sequence for 8-b5rev
- SEQ ID NO: 214 is the determined cDNA sequence for 8-b6fwd
- SEQ ID NO: 215 is the determined cDNA sequence for 8-b6 rev
- SEQ ID NO: 216 is the determined cDNA sequence for 8-d4fwd
- 20 SEQ ID NO: 217 is the determined cDNA sequence for 8-d9rev
- SEQ ID NO: 218 is the determined cDNA sequence for 8-g3fwd
- SEQ ID NO: 219 is the determined cDNA sequence for 8-g3rev
- SEQ ID NO: 220 is the determined cDNA sequence for 8-h11rev
- SEQ ID NO: 221 is the determined cDNA sequence for g-f12fwd
- 25 SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev
- SEQ ID NO: 223 is the determined cDNA sequence for P509S
- SEQ ID NO: 224 is the determined cDNA sequence for P510S
- SEQ ID NO: 225 is the determined cDNA sequence for P703DE5
- SEQ ID NO: 226 is the determined cDNA sequence for 9-A11
- 30 SEQ ID NO: 227 is the determined cDNA sequence for 8-C6
- SEQ ID NO: 228 is the determined cDNA sequence for 8-H7
- SEQ ID NO: 229 is the determined cDNA sequence for JPTPN13

- SEQ ID NO: 230 is the determined cDNA sequence for JPTPN14
SEQ ID NO: 231 is the determined cDNA sequence for JPTPN23
SEQ ID NO: 232 is the determined cDNA sequence for JPTPN24
SEQ ID NO: 233 is the determined cDNA sequence for JPTPN25
5 SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30
SEQ ID NO: 235 is the determined cDNA sequence for JPTPN34
SEQ ID NO: 236 is the determined cDNA sequence for PTPN35
SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36
SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38
10 SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39
SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40
SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41
SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42
SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45
15 SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46
SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51
SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56
SEQ ID NO: 247 is the determined cDNA sequence for PTPN64
SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65
20 SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67
SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76
SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84
SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85
SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86
25 SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87
SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88
SEQ ID NO: 256 is the determined cDNA sequence for JP1F1
SEQ ID NO: 257 is the determined cDNA sequence for JP1F2
SEQ ID NO: 258 is the determined cDNA sequence for JP1C2
30 SEQ ID NO: 259 is the determined cDNA sequence for JP1B1
SEQ ID NO: 260 is the determined cDNA sequence for JP1B2
SEQ ID NO: 261 is the determined cDNA sequence for JP1D3

- SEQ ID NO: 262 is the determined cDNA sequence for JP1A4
SEQ ID NO: 263 is the determined cDNA sequence for JP1F5
SEQ ID NO: 264 is the determined cDNA sequence for JP1E6
SEQ ID NO: 265 is the determined cDNA sequence for JP1D6
5 SEQ ID NO: 266 is the determined cDNA sequence for JP1B5
SEQ ID NO: 267 is the determined cDNA sequence for JP1A6
SEQ ID NO: 268 is the determined cDNA sequence for JP1E8
SEQ ID NO: 269 is the determined cDNA sequence for JP1D7
SEQ ID NO: 270 is the determined cDNA sequence for JP1D9
10 SEQ ID NO: 271 is the determined cDNA sequence for JP1C10
SEQ ID NO: 272 is the determined cDNA sequence for JP1A9
SEQ ID NO: 273 is the determined cDNA sequence for JP1F12
SEQ ID NO: 274 is the determined cDNA sequence for JP1E12
SEQ ID NO: 275 is the determined cDNA sequence for JP1D11
15 SEQ ID NO: 276 is the determined cDNA sequence for JP1C11
SEQ ID NO: 277 is the determined cDNA sequence for JP1C12
SEQ ID NO: 278 is the determined cDNA sequence for JP1B12
SEQ ID NO: 279 is the determined cDNA sequence for JP1A12
SEQ ID NO: 280 is the determined cDNA sequence for JP8G2
20 SEQ ID NO: 281 is the determined cDNA sequence for JP8H1
SEQ ID NO: 282 is the determined cDNA sequence for JP8H2
SEQ ID NO: 283 is the determined cDNA sequence for JP8A3
SEQ ID NO: 284 is the determined cDNA sequence for JP8A4
SEQ ID NO: 285 is the determined cDNA sequence for JP8C3
25 SEQ ID NO: 286 is the determined cDNA sequence for JP8G4
SEQ ID NO: 287 is the determined cDNA sequence for JP8B6
SEQ ID NO: 288 is the determined cDNA sequence for JP8D6
SEQ ID NO: 289 is the determined cDNA sequence for JP8F5
SEQ ID NO: 290 is the determined cDNA sequence for JP8A8
30 SEQ ID NO: 291 is the determined cDNA sequence for JP8C7
SEQ ID NO: 292 is the determined cDNA sequence for JP8D7
SEQ ID NO: 293 is the determined cDNA sequence for P8D8

- SEQ ID NO: 294 is the determined cDNA sequence for JP8E7
SEQ ID NO: 295 is the determined cDNA sequence for JP8F8
SEQ ID NO: 296 is the determined cDNA sequence for JP8G8
SEQ ID NO: 297 is the determined cDNA sequence for JP8B10
5 SEQ ID NO: 298 is the determined cDNA sequence for JP8C10
SEQ ID NO: 299 is the determined cDNA sequence for JP8E9
SEQ ID NO: 300 is the determined cDNA sequence for JP8E10
SEQ ID NO: 301 is the determined cDNA sequence for JP8F9
SEQ ID NO: 302 is the determined cDNA sequence for JP8H9
10 SEQ ID NO: 303 is the determined cDNA sequence for JP8C12
SEQ ID NO: 304 is the determined cDNA sequence for JP8E11
SEQ ID NO: 305 is the determined cDNA sequence for JP8E12
SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12
SEQ ID NO: 307 is the determined cDNA sequence for P711P
15 SEQ ID NO: 308 is the determined cDNA sequence for P712P
SEQ ID NO: 309 is the determined cDNA sequence for CLONE23
SEQ ID NO: 310 is the determined cDNA sequence for P774P
SEQ ID NO: 311 is the determined cDNA sequence for P775P
SEQ ID NO: 312 is the determined cDNA sequence for P715P
20 SEQ ID NO: 313 is the determined cDNA sequence for P710P
SEQ ID NO: 314 is the determined cDNA sequence for P767P
SEQ ID NO: 315 is the determined cDNA sequence for P768P
SEQ ID NO: 316-325 are the determined cDNA sequences of previously isolated genes
SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5
25 SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5
SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26
SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26
SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23
SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23
30 SEQ ID NO: 332 is the determined full length cDNA sequence for P509S
SEQ ID NO: 333 is the determined extended cDNA sequence for P707P (also referred to as 11-C9)
SEQ ID NO: 334 is the determined cDNA sequence for P714P

- SEQ ID NO: 335 is the determined cDNA sequence for P705P (also referred to as 9-F3)
- SEQ ID NO: 336 is the predicted amino acid sequence for P705P
- SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10
- SEQ ID NO: 338 is the amino acid sequence of the peptide p5
- 5 SEQ ID NO: 339 is the predicted amino acid sequence of P509S
- SEQ ID NO: 340 is the determined cDNA sequence for P778P
- SEQ ID NO: 341 is the determined cDNA sequence for P786P
- SEQ ID NO: 342 is the determined cDNA sequence for P789P
- SEQ ID NO: 343 is the determined cDNA sequence for a clone showing homology to Homo
- 10 sapiens MM46 mRNA
- SEQ ID NO: 344 is the determined cDNA sequence for a clone showing homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA
- SEQ ID NO: 345 is the determined cDNA sequence for a clone showing homology to Homo sapiens mRNA for E-cadherin
- 15 SEQ ID NO: 346 is the determined cDNA sequence for a clone showing homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase (SHMT)
- SEQ ID NO: 347 is the determined cDNA sequence for a clone showing homology to Homo sapiens natural resistance-associated macrophage protein2 (NRAMP2)
- SEQ ID NO: 348 is the determined cDNA sequence for a clone showing homology to Homo
- 20 sapiens phosphoglucomutase-related protein (PGMRP)
- SEQ ID NO: 349 is the determined cDNA sequence for a clone showing homology to Human mRNA for proteosome subunit p40
- SEQ ID NO: 350 is the determined cDNA sequence for P777P
- SEQ ID NO: 351 is the determined cDNA sequence for P779P
- 25 SEQ ID NO: 352 is the determined cDNA sequence for P790P
- SEQ ID NO: 353 is the determined cDNA sequence for P784P
- SEQ ID NO: 354 is the determined cDNA sequence for P776P
- SEQ ID NO: 355 is the determined cDNA sequence for P780P
- SEQ ID NO: 356 is the determined cDNA sequence for P544S
- 30 SEQ ID NO: 357 is the determined cDNA sequence for P745S
- SEQ ID NO: 358 is the determined cDNA sequence for P782P
- SEQ ID NO: 359 is the determined cDNA sequence for P783P

- SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984
- SEQ ID NO: 361 is the determined cDNA sequence for P787P
- SEQ ID NO: 362 is the determined cDNA sequence for P788P
- SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994
- 5 SEQ ID NO: 364 is the determined cDNA sequence for P781P
- SEQ ID NO: 365 is the determined cDNA sequence for P785P
- SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.
- SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 366.
- 10 SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372.
- SEQ ID NO: 378 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 373.
- SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 374.
- 15 SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 375.
- SEQ ID NO: 381 is the determined cDNA sequence for B716P.
- SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.
- 20 SEQ ID NO: 383 is the predicted amino acid sequence for P711P.
- SEQ ID NO: 384 is the cDNA sequence for P1000C.
- SEQ ID NO: 385 is the cDNA sequence for CGI-82.
- SEQ ID NO: 386 is the cDNA sequence for 23320.
- SEQ ID NO: 387 is the cDNA sequence for CGI-69.
- 25 SEQ ID NO: 388 is the cDNA sequence for L-iditol-2-dehydrogenase.
- SEQ ID NO: 389 is the cDNA sequence for 23379.
- SEQ ID NO: 390 is the cDNA sequence for 23381.
- SEQ ID NO: 391 is the cDNA sequence for KIAA0122.
- SEQ ID NO: 392 is the cDNA sequence for 23399.
- 30 SEQ ID NO: 393 is the cDNA sequence for a previously identified gene.
- SEQ ID NO: 394 is the cDNA sequence for HCLBP.
- SEQ ID NO: 395 is the cDNA sequence for transglutaminase.

SEQ ID NO:396 is the cDNA sequence for a previously identified gene.

SEQ ID NO:397 is the cDNA sequence for PAP.

SEQ ID NO:398 is the cDNA sequence for Ets transcription factor PDEF.

SEQ ID NO:399 is the cDNA sequence for hTGR.

5 SEQ ID NO:400 is the cDNA sequence for KIAA0295.

SEQ ID NO:401 is the cDNA sequence for 22545.

SEQ ID NO:402 is the cDNA sequence for 22547.

SEQ ID NO:403 is the cDNA sequence for 22548.

SEQ ID NO:404 is the cDNA sequence for 22550.

10 SEQ ID NO:405 is the cDNA sequence for 22551.

SEQ ID NO:406 is the cDNA sequence for 22552.

SEQ ID NO:407 is the cDNA sequence for 22553.

SEQ ID NO:408 is the cDNA sequence for 22558.

SEQ ID NO:409 is the cDNA sequence for 22562.

15 SEQ ID NO:410 is the cDNA sequence for 22565.

SEQ ID NO:411 is the cDNA sequence for 22567.

SEQ ID NO:412 is the cDNA sequence for 22568.

SEQ ID NO:413 is the cDNA sequence for 22570.

SEQ ID NO:414 is the cDNA sequence for 22571.

20 SEQ ID NO:415 is the cDNA sequence for 22572.

SEQ ID NO:416 is the cDNA sequence for 22573.

SEQ ID NO:417 is the cDNA sequence for 22573.

SEQ ID NO:418 is the cDNA sequence for 22575.

SEQ ID NO:419 is the cDNA sequence for 22580.

25 SEQ ID NO:420 is the cDNA sequence for 22581.

SEQ ID NO:421 is the cDNA sequence for 22582.

SEQ ID NO:422 is the cDNA sequence for 22583.

SEQ ID NO:423 is the cDNA sequence for 22584.

SEQ ID NO:424 is the cDNA sequence for 22585.

30 SEQ ID NO:425 is the cDNA sequence for 22586.

SEQ ID NO:426 is the cDNA sequence for 22587.

SEQ ID NO:427 is the cDNA sequence for 22588.

- SEQ ID NO:428 is the cDNA sequence for 22589.
SEQ ID NO:429 is the cDNA sequence for 22590.
SEQ ID NO:430 is the cDNA sequence for 22591.
SEQ ID NO:431 is the cDNA sequence for 22592.
5 SEQ ID NO:432 is the cDNA sequence for 22593.
SEQ ID NO:433 is the cDNA sequence for 22594.
SEQ ID NO:434 is the cDNA sequence for 22595.
SEQ ID NO:435 is the cDNA sequence for 22596.
SEQ ID NO:436 is the cDNA sequence for 22847.
10 SEQ ID NO:437 is the cDNA sequence for 22848.
SEQ ID NO:438 is the cDNA sequence for 22849.
SEQ ID NO:439 is the cDNA sequence for 22851.
SEQ ID NO:440 is the cDNA sequence for 22852.
SEQ ID NO:441 is the cDNA sequence for 22853.
15 SEQ ID NO:442 is the cDNA sequence for 22854.
SEQ ID NO:443 is the cDNA sequence for 22855.
SEQ ID NO:444 is the cDNA sequence for 22856.
SEQ ID NO:445 is the cDNA sequence for 22857.
SEQ ID NO:446 is the cDNA sequence for 23601.
20 SEQ ID NO:447 is the cDNA sequence for 23602.
SEQ ID NO:448 is the cDNA sequence for 23605.
SEQ ID NO:449 is the cDNA sequence for 23606.
SEQ ID NO:450 is the cDNA sequence for 23612.
SEQ ID NO:451 is the cDNA sequence for 23614.
25 SEQ ID NO:452 is the cDNA sequence for 23618.
SEQ ID NO:453 is the cDNA sequence for 23622.
SEQ ID NO:454 is the cDNA sequence for folate hydrolase.
SEQ ID NO:455 is the cDNA sequence for LIM protein.
SEQ ID NO:456 is the cDNA sequence for a known gene.
30 SEQ ID NO:457 is the cDNA sequence for a known gene.
SEQ ID NO:458 is the cDNA sequence for a previously identified gene.
SEQ ID NO:459 is the cDNA sequence for 23045.

SEQ ID NO:460 is the cDNA sequence for 23032.

SEQ ID NO:461 is the cDNA sequence for 23054.

SEQ ID NO:462-467 are cDNA sequences for known genes.

SEQ ID NO:468-471 are cDNA sequences for P710P.

- 5 SEQ ID NO:472 is a cDNA sequence for P1001C.

SEQ ID NO: 473 is the determined cDNA sequence for a first splice variant of P775P (referred to as 27505).

SEQ ID NO: 474 is the determined cDNA sequence for a second splice variant of P775P (referred to as 19947).

- 10 SEQ ID NO: 475 is the determined cDNA sequence for a third splice variant of P775P (referred to as 19941).

SEQ ID NO: 476 is the determined cDNA sequence for a fourth splice variant of P775P (referred to as 19937).

- 15 SEQ ID NO: 477 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.

SEQ ID NO: 478 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.

SEQ ID NO: 479 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 475.

- 20 SEQ ID NO: 480 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 481 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

- 25 SEQ ID NO: 482 is a third predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 483 is a fourth predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 484 is the first 30 amino acids of the *M. tuberculosis* antigen Ra12.

SEQ ID NO: 485 is the PCR primer AW025.

- 30 SEQ ID NO: 486 is the PCR primer AW003.

SEQ ID NO: 487 is the PCR primer AW027.

SEQ ID NO: 488 is the PCR primer AW026.

- SEQ ID NO: 489-501 are peptides employed in epitope mapping studies.
- SEQ ID NO: 502 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody 20D4.
- SEQ ID NO: 503 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody JA1.
- SEQ ID NO: 504 & 505 are peptides employed in epitope mapping studies.
- SEQ ID NO: 506 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 8H2.
- SEQ ID NO: 507 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 7H8.
- SEQ ID NO: 508 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 2D4.
- SEQ ID NO: 509-522 are peptides employed in epitope mapping studies.
- SEQ ID NO: 523 is a mature form of P703P used to raise antibodies against P703P. SEQ ID NO: 524 is the putative full-length cDNA sequence of P703P.
- SEQ ID NO: 525 is the predicted amino acid sequence encoded by SEQ ID NO: 524.
- SEQ ID NO: 526 is the full-length cDNA sequence for P790P.
- SEQ ID NO: 527 is the predicted amino acid sequence for P790P.
- SEQ ID NO: 528 & 529 are PCR primers.
- SEQ ID NO: 530 is the cDNA sequence of a splice variant of SEQ ID NO: 366.
- SEQ ID NO: 531 is the cDNA sequence of the open reading frame of SEQ ID NO: 530.
- SEQ ID NO: 532 is the predicted amino acid encoded by the sequence of SEQ ID NO: 531.
- SEQ ID NO: 533 is the DNA sequence of a putative ORF of P775P.
- SEQ ID NO: 534 is the predicted amino acid sequence encoded by SEQ ID NO: 533.
- SEQ ID NO: 535 is a first full-length cDNA sequence for P510S.
- SEQ ID NO: 536 is a second full-length cDNA sequence for P510S.
- SEQ ID NO: 537 is the predicted amino acid sequence encoded by SEQ ID NO: 535.
- SEQ ID NO: 538 is the predicted amino acid sequence encoded by SEQ ID NO: 536.
- SEQ ID NO: 539 is the peptide P501S-370.
- SEQ ID NO: 540 is the peptide P501S-376.
- SEQ ID NO: 541-550 are epitopes of P501S.
- SEQ ID NO: 551 corresponds to amino acids 543-553 of P501S.

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer. The compositions described herein may include prostate-specific polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (*e.g.*, T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a prostate-specific protein or a variant thereof. A "prostate-specific protein" is a protein that is expressed in normal prostate and/or prostate tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a non-prostate normal tissue, as determined using a representative assay provided herein. Certain prostate-specific proteins are proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with prostate cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery of human prostate-specific proteins. Sequences of polynucleotides encoding certain prostate-specific proteins, or portions thereof, are provided in SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536. Sequences of polypeptides comprising at least a portion of a prostate-specific protein are provided in SEQ ID NOs: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534 and 537-550.

PROSTATE-SPECIFIC PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a prostate-specific protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred

polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a prostate-specific protein. More preferably, a polynucleotide encodes an immunogenic portion of a prostate-specific protein. Polynucleotides complementary to any such sequences are also
5 encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the
10 present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a prostate-specific protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions
15 and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native prostate-specific protein or a portion thereof. The
20 term "variants" also encompasses homologous genes of xenogenic origin.

Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local
25 regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the
30 Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices

for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenesis pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native prostate-specific protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such

as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least five fold greater in a prostate-specific than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as prostate-specific cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

An amplified portion may be used to isolate a full length gene from a suitable library (*e.g.*, a prostate-specific cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (*e.g.*, by nick-translation or end-labeling with ^{32}P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (*see* Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into

a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments; using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (*see* Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids. Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (*e.g.*, NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

Certain nucleic acid sequences of cDNA molecules encoding at least a portion of a prostate-specific protein are provided in SEQ ID NO:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536.

Isolation of these polynucleotides is described below. Each of these prostate-specific proteins was overexpressed in prostate tumor tissue.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis.

5 Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (*see* Adelman et al., *DNA* 2:183, 1983). Alternatively, RNA molecules may be generated by *in vitro* or *in vivo* transcription of DNA sequences encoding a prostate-specific protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain
10 portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated *in vivo* (*e.g.*, by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a prostate-specific polypeptide, and administering the transfected cells to the patient).

15 A portion of a sequence complementary to a coding sequence (*i.e.*, an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a protein. Antisense technology can be used to control gene expression
20 through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (*see* Gee et al., *In* Huber and Carr, *Molecular and Immunologic Approaches*, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (*e.g.*, promoter, enhancer or transcription initiation site), and block transcription of
25 the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30
30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3'

ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

5 Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In general, a vector
10 will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for
15 therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (*e.g.*, avian pox virus). The polynucleotides may also be administered as naked plasmid vectors.
20 Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary
25 skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane
30 vesicle). The preparation and use of such systems is well known in the art.

PROSTATE-SPECIFIC POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a prostate-specific protein or a variant thereof, as described herein. As noted above, a "prostate-specific protein" is a protein that is expressed by normal prostate and/or prostate tumor cells. Proteins that are prostate-specific proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with prostate cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a prostate-specific protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native prostate-specific protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the

immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ¹²⁵I-labeled Protein A.

As noted above, a composition may comprise a variant of a native prostate-specific protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native prostate-specific protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (e.g., 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein. Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydrophobic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino

acids that have minimal influence on the immunogenicity, secondary structure and hydrophobic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (*e.g.*, poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast, higher eukaryotic and plant cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known prostate-specific protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner),

preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are

located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (*see, for example, Stoute et al. New Engl. J. Med., 336:86-91, 1997*).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its

original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector
5 that is not a part of the natural environment.

BINDING AGENTS

The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a prostate-specific protein. As used herein, an
10 antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a prostate-specific protein if it reacts at a detectable level (within, for example, an ELISA) with a prostate-specific protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding
15 constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about 10^3 L/mol. The binding constant may be determined using methods well known in the art.

20 Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a prostate-specific protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals
25 without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (*e.g.*, blood, sera, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the
30 above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Most preferably, antibodies employed in the inventive methods have the ability to induce lysis of tumor cells by activation of complement and mediation of antibody-dependent cellular cytotoxicity (ADCC). Antibodies of different classes and subclasses differ in these properties. For example, mouse antibodies of the IgG2a and IgG3 classes are capable of activating serum complement upon binding to target cells which express the antigen against which the antibodies were raised, and can mediate ADCC.

Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (i.e., reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells

and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are
5 selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse.
10 Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

The preparation of mouse and rabbit monoclonal antibodies that specifically bind to
15 polypeptides of the present invention is described in detail below. However, the antibodies of the present invention are not limited to those derived from mice. Human antibodies may also be employed in the inventive methods and may prove to be preferable. Such antibodies can be obtained using human hybridomas as described by Cote *et al.* (Monoclonal Antibodies and Cancer Therapy, Alan R. Lisa, p. 77, 1985). The present invention also encompasses antibodies made by
20 recombinant means such as chimeric antibodies, wherein the variable region and constant region are derived from different species, and CDR-grafted antibodies, wherein the complementarity determining region is derived from a different species, as described in US Patents 4,816,567 and 5,225,539. Chimeric antibodies may be prepared by splicing genes for a mouse antibody molecule having a desired antigen specificity together with genes for a human antibody molecule having the
25 desired biological activity, such as activation of human complement and mediation of ADCC (Morrison *et al. Proc. Natl. Acad. Sci. USA* 81:6851, 1984; Neuberger *et al. Nature* 312:604, 1984; Takeda *et al. Nature* 314:452, 1985).

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard
30 techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, *Antibodies: A Laboratory Manual*,

Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ^{90}Y , ^{123}I , ^{125}I , ^{131}I , ^{186}Re , ^{188}Re , ^{211}At , and ^{212}Bi . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to

Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

5 It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or
10 linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent
15 No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating
20 compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of
25 a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

T CELLS

30 Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a prostate-specific protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral

blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the ISOLEX™ system, available from Nexell Therapeutics Inc., Irvine, CA (see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated
5 humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a prostate-specific polypeptide, polynucleotide encoding a prostate-specific polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a prostate-specific
10 polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a prostate-specific polypeptide if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a
15 variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell
20 proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a prostate-specific polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of
25 the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-γ) is indicative of T cell activation (see Coligan et al., *Current Protocols in Immunology*, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a prostate-specific polypeptide, polynucleotide or polypeptide-expressing APC may be CD4⁺ and/or CD8⁺. Prostate-specific protein-specific T cells may be expanded using
30 standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4⁺ or CD8⁺ T cells that proliferate in response to a prostate-specific polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a prostate-specific polypeptide, or a short peptide
5 corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a prostate-specific polypeptide. Alternatively, one or more T cells that proliferate in the presence of a prostate-specific protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

10

PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds
15 and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and an immunostimulant. An immunostimulant may be any substance that enhances an immune response to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally
20 described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the
25 composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression
30 systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression

in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA

or glutathione, adjuvants (*e.g.*, aluminum hydroxide) and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (*e.g.*, IFN- γ , TNF α , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (*e.g.*, IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT; *see* US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example,

an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent
5 adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release
10 formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix
15 and/or contained within a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

20 Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the
25 antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or
30 progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy,

Ann. Rev. Med. 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take-up, process and present antigens with high efficiency, and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface
5 receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone
10 marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF α to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into
15 dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF α , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this
20 nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc γ receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II
25 MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide encoding a prostate-specific protein (or portion or other variant thereof) such that the prostate-specific polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex*
30 *vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection

that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells
5 with the prostate-specific polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of
10 the polypeptide.

CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as prostate cancer. Within such methods, pharmaceutical
15 compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor.
20 Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react
25 against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not
30 necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8⁺ cytotoxic T lymphocytes and CD4⁺ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer

cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate
5 antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in*
10 *vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte,
15 fibroblast or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies
20 have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see*, for example, Cheever et al., *Immunological Reviews* 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back
25 into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established
30 using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered

over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50%
5 above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-
10 vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25 μ g to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active
15 compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a prostate-specific protein generally correlate with an improved clinical outcome. Such immune responses may generally be
20 evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or
25 more prostate-specific proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the
30 agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer.

In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. *See, e.g., Harlow and Lane, 5 Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized
10 on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G,
15 protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full
20 length prostate-specific proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or
25 disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization"
30 refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a

membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of
5 binding agent ranging from about 10 ng to about 10 μ g, and preferably about 100 ng to about 1 μ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the
10 binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.*, Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may
15 be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The
20 amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween
25 20TM (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer.
30 Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by

assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains
5 a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of
10 time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group
15 (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a
20 signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is
25 determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest
30 to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along

the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 μ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use prostate-specific polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such prostate-specific protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a prostate-specific protein in a biological sample. Within certain methods, a biological sample comprising CD4⁺ and/or CD8⁺ T cells isolated from a patient is incubated with a prostate-specific polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that

expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may
5 be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with prostate-specific polypeptide (*e.g.*, 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of prostate-specific polypeptide to serve as a control. For CD4⁺ T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater
10 and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a prostate-specific protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to
15 amplify a portion of a prostate-specific cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the prostate-specific protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a prostate-specific protein may be used in a hybridization
20 assay to detect the presence of polynucleotide encoding the protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a prostate-specific protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in
25 length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15
30 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536. Techniques for both PCR based assays and hybridization assays

are well known in the art (*see*, for example, Mullis et al., *Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple prostate-specific protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for proteins provided herein may be combined with assays for other known tumor antigens.

DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a prostate-specific protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a prostate-specific protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a prostate-specific protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a prostate-specific protein.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLES

EXAMPLE 1

5 ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from prostate
10 tumor poly A⁺ RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning
kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol.
Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and
total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the
manufacturer. The poly A⁺ RNA was then purified using a Qiagen oligotex spin column mRNA
15 purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-
strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was
synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with
NotI. Following size fractionation with Chroma Spin-1000 columns (Clontech, Palo Alto, CA), the
cDNA was ligated into the EcoRI/NotI site of pCDNA3.1 (Invitrogen) and transformed into
20 ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was
prepared from a pool of six tissue specimens (Clontech). The cDNA libraries were characterized by
determining the number of independent colonies, the percentage of clones that carried insert, the
average insert size and by sequence analysis. The prostate tumor library contained 1.64×10^7
25 independent colonies, with 70% of clones having an insert and the average insert size being 1745
base pairs. The normal pancreas cDNA library contained 3.3×10^6 independent colonies, with 69%
of clones having inserts and the average insert size being 1120 base pairs. For both libraries,
sequence analysis showed that the majority of clones had a full length cDNA sequence and were
synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

30 cDNA library subtraction was performed using the above prostate tumor and normal
pancreas cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some
modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as

follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, NotI, and SfuI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 100 µl of H₂O, heat-denatured and mixed with 100 µl (100 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As
5 recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 µl H₂O to form the driver DNA.

To form the tracer DNA, 10 µg prostate tumor cDNA library was digested with
10 BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 µl H₂O. Tracer DNA was mixed with 15 µl driver DNA and 20 µl of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and
15 incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 µl H₂O, mixed with 8 µl driver DNA and 20 µl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA
20 was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK⁺ (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and
25 grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively,
30 with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12. This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1 μ g each of human glandular kallikrein, PSA and mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively). Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to *R. norvegicus* mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA

library with spike, four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show
5 some homology to known human sequences. No significant homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding predicted amino acid
10 sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided
15 in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein,
20 mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in
30 SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated

clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807, 1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were over-expressed in most prostate tumors and prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the identification of six additional clones referred to as 1G-4761, 1G-4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 199, respectively, and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA⁺ RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297, 1D-4309, 1D-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni,

Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional, studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339. Two variant full-length cDNA sequences for P510S are provided in SEQ ID NO: 535 and 536, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 537 and 538, respectively.

EXAMPLE 2

DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE-SPECIFIC POLYPEPTIDES

Using gene specific primers, mRNA expression levels for the representative prostate-specific polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 1-2 μ g of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β -actin was used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed using β -actin specific primers. A dilution was then chosen that enabled the linear range amplification of the β -actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β -actin levels were determined for each

reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in four different types of tumor tissue
5 (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found
10 to be expressed at high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other
15 tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of
20 prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

25 RT-PCR characterization of R1-2330, U1-3064 and ID-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH
prostates, and normal colon, kidney, liver, lung, pancreas, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors
30 and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney,

but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following
5 normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues
10 tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal prostate, expressed at lower levels in
15 normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in
20 prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmataziz *et al.* (*Proc. Natl. Acad. Sci. USA* 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and
25 expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was
30 found to show some homology to the previously isolated Human mRNA for JM27 protein. No significant homologies were found to the sequence of P1000C.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver, brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

20

EXAMPLE 3

ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA subtraction library, containing cDNA from normal prostate subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' *E. coli* (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences
5 for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

Further studies using the PCR-based methodology described above resulted in the
10 isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145, 147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-
15 170) were found to have some degree of homology to known genes. Larger cDNA clones containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA
20 sequence for an extended spliced form of P703 is provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary
25 (n=2), skeletal muscle, skin, stomach, small intestine and brain), and activated and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed comparable expression. P20, a
30 portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of

2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal prostate and prostate tumor, compared to six of twelve other normal tissues tested. Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However, substantial expression of P29 was observed in normal colon and normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

mRNA expression levels for these clones were determined using the micro-array technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable. Increased expression of 8-F11 was seen in prostate tumor and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.

An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both micro-array technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those in the public databases revealed 99% identity to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

PCR and hybridization-based methodologies were employed to obtain longer cDNA sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX_23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of the putative signal sequence. The putative full-length cDNA sequence for P703P is provided in SEQ ID NO: 524, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 525.

Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are provided in SEQ ID NO: 307-311, 313 and 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold over-expression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal prostate tissues (n=4), but background to low expression levels in all normal tissues. Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no significant homologies to P714P were found.

Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

Further studies on P775P resulted in the isolation of four additional sequences (SEQ ID NO: 473-476) which are all splice variants of the P775P gene. The sequence of SEQ ID NO: 474 was found to contain two open reading frames (ORFs). The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 477 and 478. The cDNA sequence of SEQ ID NO: 475 was found to contain an ORF which encodes the amino acid sequence of SEQ ID NO: 479. The cDNA sequence of SEQ ID NO: 473 was found to contain four ORFs. The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 480-483.

Subsequent studies led to the identification of a genomic region on chromosome 22q11.2, known as the Cat Eye Syndrome region, that contains the five prostate genes P704P, P712P, P774P, P775P and B305D. The relative location of each of these five genes within the genomic region is shown in Fig. 10. This region may therefore be associated with malignant tumors, and other potential tumor genes may be contained within this region. These studies also led

to the identification of a potential open reading frame (ORF) for P775P (provided in SEQ ID NO: 533), which encodes the amino acid sequence of SEQ ID NO: 534.

EXAMPLE 4

SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using FMOC chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

EXAMPLE 5

FURTHER ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that recognize six-nucleotide restriction sites (MluI, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the

subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat *norvegicus* cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to *G. gallus* dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most

recent release of GenBank revealed no significant homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most prostate tumors and BPH tissues by a factor of three or greater, with elevated expression seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low expression in all other normal tissues tested.

Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349, 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 10 (SEQ ID NO: 340-349) were found to show some homology to previously identified sequences. No significant homologies were found to the clones of SEQ ID NO: 350, 351 and 353-365.

Further studies on the clone of SEQ ID NO: 352 (referred to as P790P) led to the isolation of the full-length cDNA sequence of SEQ ID NO: 526. The corresponding predicted amino acid is provided in SEQ ID NO: 527. Data from two quantitative PCR experiments indicated that P790P is over-expressed in 11/15 tested prostate tumor samples and is expressed at low levels in spinal cord, with no expression being seen in all other normal samples tested. Data from further PCR experiments and microarray experiments showed over-expression in normal prostate and prostate tumor with little or no expression in other tissues tested. P790P was subsequently found to show significant homology to a previously identified G-protein coupled prostate tissue receptor.

EXAMPLE 6

PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

5 6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

Mice expressing the transgene for human HLA A2Kb (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID
10 NO: 8), as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were immunized with 100µg of P2S#12 and 120µg of an I-A^b binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at 6×10^6 cells/ml in complete media (RPMI-1640; Gibco
15 BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL), 2×10^{-5} M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later, cells ($5 \times$
20 10^5 /ml) were restimulated with 2.5×10^6 /ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, *Science* 258:815-818, 1992) and 3×10^6 /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb
25 tumor cells (1×10^4 cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5×10^5 cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2Kb expressing) transduced with P502S than against control fibroblasts. An example is presented in
30 Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2Kb molecule.

6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, *et al*, *J. Immunol.*, 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200 µg/ml were added to cultures of D150M58 CTL in order to bind HLA-A2 on the CTL. After thirty minutes, CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

Mice expressing the transgene for human HLA A2Kb were immunized as described by Theobald et al. (*Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5µg of P1S #10 and 120µg of an I-A^b binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared using a nylon mesh. Cells were then resuspended at 6×10^6 cells/ml in complete media (as described above) and cultured in the presence of irradiated (3000 rads) P1S#10-pulsed (2µg/ml P1S#10 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later cells (5×10^5 /ml) were restimulated with 2.5×10^6 /ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and 3×10^6 /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were restimulated on a weekly basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1×10^4 cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5×10^5 cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were isolated and maintained in culture. As shown
5 in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

EXAMPLE 7

10 PRIMING OF CTL *IN VIVO* USING NAKED DNA IMMUNIZATION WITH A PROSTATE ANTIGEN

The prostate-specific antigen L1-12, as described above, is also referred to as P501S. HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with 100 μ g P501S in the vector VR1012 either intramuscularly or intradermally.
15 The mice were immunized three times, with a two week interval between immunizations. Two weeks after the last immunization, immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL activity was assessed against P501S transduced targets. Two out of 8 mice developed strong anti-P501S CTL responses. These results demonstrate that P501S contains at
20 least one naturally processed HLA-A2-restricted CTL epitope.

EXAMPLE 8

25 ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE-SPECIFIC POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate tumor polypeptide to recognize human tumor.

Human CD8⁺ T cells were primed *in vitro* to the P2S-12 peptide (SEQ ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells according to the protocol of Van
30 Tsai et al. (*Critical Reviews in Immunology* 18:65-75, 1998). The resulting CD8⁺ T cell microcultures were tested for their ability to recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which were transduced to express the P502S gene in a γ -interferon

ELISPOT assay (*see* Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). Briefly, titrating numbers of T cells were assayed in duplicate on 10^4 fibroblasts in the presence of 3 $\mu\text{g/ml}$ human β_2 -microglobulin and 1 $\mu\text{g/ml}$ P2S-12 peptide or control E75 peptide. In addition, T cells were simultaneously assayed on autologous fibroblasts transduced with the P502S gene or as a control, fibroblasts transduced with HER-2/*neu*. Prior to the assay, the fibroblasts were treated with 10 ng/ml γ -interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a γ -interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of γ -interferon spots with increasing numbers of T cells on fibroblasts pulsed with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of γ -interferon spots with increasing numbers of T cells on fibroblasts transduced to express the P502S gene but not the HER-2/*neu* gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

EXAMPLE 9

ELICITATION OF PROSTATE ANTIGEN-SPECIFIC CTL RESPONSES IN HUMAN BLOOD

This Example illustrates the ability of a prostate-specific antigen to elicit a CTL response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GM-CSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8⁺ cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles using autologous fibroblasts retrovirally transduced

to express P501S and CD80, CD8+ lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL transduced to express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxicity assays (⁵¹Cr release) and interferon-gamma production (Interferon-gamma Elispot; see above and Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). The results of these assays are presented in Figures 6A and 6B.

EXAMPLE 10

IDENTIFICATION OF A NATURALLY PROCESSED CTL EPITOPE CONTAINED WITHIN A PROSTATE-SPECIFIC ANTIGEN

The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific human CD8+ T cells can be primed following repeated *in vitro* stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed and P703P-transduced target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2Kb transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of HLA-A2Kb or HLA-A2 transduced target cells expressing P703P.

Initial studies demonstrating that p5 is a naturally processed epitope were done using HLA-A2Kb transgenic mice. HLA-A2Kb transgenic mice were immunized subcutaneously in the footpad with 100 µg of p5 peptide together with 140 µg of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated *in vitro* with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary *in vitro* stimulation. Retrovirally transduced cells expressing the control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were identified.

Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte cultures derived

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Using *in vitro* whole-gene priming with P501S-vaccinia infected DC (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996), human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon- γ ELISPOT analysis as described above. Using a panel of
5 HLA-mismatched B-LCL lines transduced with P501S, these CTL lines were shown to be likely restricted to HLAB class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a
10 multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3 μ g/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8⁺ T cells were isolated using a magnetic bead system, and priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S and CD80. Following four stimulation cycles, CD8⁺ T cell lines were identified that
15 specifically produced interferon- γ when stimulated with P501S and CD80-transduced autologous fibroblasts. A panel of HLA-mismatched B-LCL lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon- γ in an ELISPOT assay, the P501S specific response was shown to be likely restricted by HLA B alleles. These results demonstrate that a CD8⁺ CTL response to P501S can be elicited.

20 To identify the epitope(s) recognized, cDNA encoding P501S was fragmented by various restriction digests, and sub-cloned into the retroviral expression vector pBIB-KS. Retroviral supernatants were generated by transfection of the helper packaging line Phoenix-Ampho. Supernatants were then used to transduce Jurkat/A2Kb cells for CTL screening. CTL were screened in IFN- γ ELISPOT assays against these A2Kb targets transduced with the "library" of P501S
25 fragments. Initial positive fragments P501S/H3 and P501S/F2 were sequenced and found to encode amino acids 106-553 and amino acids 136-547, respectively, of SEQ ID NO: 113. A truncation of H3 was made to encode amino acid residues 106-351 of SEQ ID NO: 113, which was unable to stimulate the CTL, thus localizing the epitope to amino acid residues 351-547. Additional fragments encoding amino acids 1-472 (Fragment A) and amino acids 1-351 (Fragment B) were
30 also constructed. Fragment A but not Fragment B stimulated the CTL thus localizing the epitope to amino acid residues 351-472. Overlapping 20-mer and 18-mer peptides representing this region were tested by pulsing Jurkat/A2Kb cells versus CTL in an IFN- γ assay. Only peptides

P501S-369(20) and P501S-369(18) stimulated the CTL. Nine-mer and 10-mer peptides representing this region were synthesized and similarly tested. Peptide P501S-370 (SEQ ID NO: 539) was the minimal 9-mer giving a strong response. Peptide P501S-376 (SEQ ID NO: 540) also gave a weak response, suggesting that it might represent a cross-reactive epitope.

5 In subsequent studies, the ability of primary human B cells transduced with P501S to prime MHC class I-restricted, P501S-specific, autologous CD8 T cells was examined. Primary B cells were derived from PBMC of a homozygous HLA-A2 donor by culture in CD40 ligand and IL-4, transduced at high frequency with recombinant P501S in the vector pBIB, and selected with blastocidin-S. For *in vitro* priming, purified CD8+ T cells were cultured with autologous CD40
10 ligand + IL-4 derived, P501S-transduced B cells in a 96-well microculture format. These CTL microcultures were re-stimulated with P501S-transduced B cells and then assayed for specificity. Following this initial screen, microcultures with significant signal above background were cloned on autologous EBV-transformed B cells (BLCL), also transduced with P501S. Using IFN-gamma ELISPOT for detection, several of these CD8 T cell clones were found to be specific for P501S, as
15 demonstrated by reactivity to BLCL/P501S but not BLCL transduced with control antigen. It was further demonstrated that the anti-P501S CD8 T cell specificity is HLA-A2-restricted. First, antibody blocking experiments with anti-HLA-A,B,C monoclonal antibody (W6.32), anti-HLA-B,C monoclonal antibody (B1.23.2) and a control monoclonal antibody showed that only the anti-HLA-A,B,C antibody blocked recognition of P501S-expressing autologous BLCL. Secondly, the anti-
20 P501S CTL also recognized an HLA-A2 matched, heterologous BLCL transduced with P501S, but not the corresponding EGFP transduced control BLCL.

EXAMPLE 13

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY ANALYSIS

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This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in
30 prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences

SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

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Table I
Summary of Prostate Tumor Antigens

Known Genes	Previously Identified Genes	Novel Genes
T-cell gamma chain	P504S	23379 (SEQ ID NO:389)
Kallikrein	P1000C	23399 (SEQ ID NO:392)
Vector	P501S	23320 (SEQ ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID NO:385)	P503S	23381 (SEQ ID NO:390)
PSA	P510S	
Ald. 6 Dehyd.	P784P	
L-iditol-2 dehydrogenase (23376; SEQ ID NO:388)	P502S	
Ets transcription factor PDEF (22672; SEQ ID NO:398)	P706P	
hTGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ ID NO:396)	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang (23404; SEQ ID NO:393)	
Prostatic Acid Phosphatase(22655; SEQ ID NO:397)	P712P	
transglutaminase (22611; SEQ ID NO:395)	P778P	
HDLBP (23508; SEQ ID NO:394)		
CGI-69 Protein(23367; SEQ ID NO:387)		
KIAA0122(23383; SEQ ID NO:391)		
TEEG		

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97%

of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

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EXAMPLE 14

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS
BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify prostate-specific antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatizis et al., *Proc. Natl. Acad. Sci. USA* 95:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups: Plus (normal prostate and prostate tumor libraries, and breast cell line libraries, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (libraries from fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which

expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

Table II

Prostate cDNA Libraries and ESTs

Library	# of Libraries	# of ESTs
Plus	25	43,482
Normal	11	18,875
Tumor	11	21,769
Cell lines	3	2,838
Minus	166	
Other	287	

Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups:

10 Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones derived from the Plus and Other group libraries only; no expression detected in the Minus group; Type 3- EST clones derived from the Plus, Minus and Other group libraries, but the number of ESTs derived from the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones derived from Plus, Minus and Other group

15 libraries, but the number derived from the Plus group is higher than the number derived from the Minus group. This analysis identified 4,345 breast clusters (*see* Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

Table III
Prostate Cluster Summary

Type	# of Superclusters	# of ESTs Ordered
1	688	677
2	2899	2484
3	85	11
4	673	0
Total	4345	3172

The EST clone inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high levels of tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

Clones with an expression ratio greater than 3 (*i.e.*, the level in prostate tumor and normal prostate mRNA was at least three times the level in other normal tissue mRNA) were identified as prostate tumor-specific sequences (Table IV). The sequences of these clones are provided in SEQ ID NO: 401-453, with certain novel sequences shown in SEQ ID NO: 407, 413, 416-419, 422, 426, 427 and 450.

Table IV
Prostate-tumor Specific Clones

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1000C
402	22547	previously identified P704P
403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57
439	22851	PAP

440	22852	PAP
441	22853	PAP
442	22854	previously identified P509S
443	22855	previously identified P705P
444	22856	previously identified P774P
445	22857	PSA
446	23601	previously identified P777P
447	23602	PSA
448	23605	PSA
449	23606	PSA
450	23612	novel
451	23614	PSA
452	23618	previously identified P1000C
453	23622	previously identified P705P

EXAMPLE 15

FURTHER IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY
ANALYSIS

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This Example describes the isolation of additional prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened
10 using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NO: 454-467. Of these sequences, SEQ ID NO: 459-461 represent novel genes. The others (SEQ ID NO: 454-458 and 461-467) correspond to known sequences.

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EXAMPLE 16

FURTHER CHARACTERIZATION OF PROSTATE-SPECIFIC ANTIGEN P710P

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This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P fragment described above. One million colonies were plated on LB/Ampicillin plates. Nylon membrane

filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic Perkin Elmer/Applied Biosystems Division Sequencer. Four
5 sequences were obtained, and are presented in SEQ ID NO: 468-471. These sequences appear to represent different splice variants of the P710P gene.

EXAMPLE 17

PROTEIN EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

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This example describes the expression and purification of the prostate-specific antigen P501S in *E. coli*, baculovirus and mammalian cells.

a) Expression in *E. coli*

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Expression of the full-length form of P501S was attempted by first cloning P501S without the leader sequence (amino acids 36-553 of SEQ ID NO: 113) downstream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) in pET17b. Specifically, P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW003 (SEQ ID NO: 486). AW025 is a sense cloning primer that contains a HindIII site. AW003 is an
20 antisense cloning primer that contains an EcoRI site. DNA amplification was performed using 5 µl 10X Pfu buffer, 1 µl 20 mM dNTPs, 1 µl each of the PCR primers at 10 µM concentration, 40 µl water, 1 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 95°C was performed for 30 sec, followed by 10 cycles of 95°C for 30 sec, 60°C for 1 min and by 72°C for 3 min. 20 cycles of 95°C for 30 sec, 65°C for 1 min and by 72°C for 3 min,
25 and lastly by 1 cycle of 72°C for 10 min. The PCR product was cloned to Ra12m/pET17b using HindIII and EcoRI. The sequence of the resulting fusion construct (referred to as Ra12-P501S-F) was confirmed by DNA sequencing.

The fusion construct was transformed into BL21(DE3)pLysE, pLysS and CodonPlus *E. coli* (Stratagene) and grown overnight in LB broth with kanamycin. The resulting culture was
30 induced with IPTG. Protein was transferred to PVDF membrane and blocked with 5% non-fat milk (in PBS-Tween buffer), washed three times and incubated with mouse anti-His tag antibody (Clontech) for 1 hour. The membrane was washed 3 times and probed with HRP-Protein A

(Zymed) for 30 min. Finally, the membrane was washed 3 times and developed with ECL (Amersham). No expression was detected by Western blot. Similarly, no expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage (Invitrogen).

5 An N-terminal fragment of P501S (amino acids 36-325 of SEQ ID NO: 113) was cloned down-stream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 in pET17b as follows. P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW027 (SEQ ID NO: 487). AW027 is an antisense cloning primer that contains an EcoRI site and a stop codon. DNA amplification was performed essentially as described above. The resulting PCR
10 product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The fusion construct (referred to as Ra12-P501S-N) was confirmed by DNA sequencing.

 The Ra12-P501S-N fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, essentially as described above. Using Western blot analysis, protein bands were observed at the expected molecular weight of 36 kDa. Some high molecular weight bands
15 were also observed, probably due to aggregation of the recombinant protein. No expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage.

 A fusion construct comprising a C-terminal portion of P501S (amino acids 257-553 of SEQ ID NO: 113) located down-stream of the first 30 amino acids of the *M. tuberculosis* antigen
20 Ra12 (SEQ ID NO: 484) was prepared as follows. P501S DNA was used to perform PCR using the primers AW026 (SEQ ID NO: 488) and AW003 (SEQ ID NO: 486). AW026 is a sense cloning primer that contains a HindIII site. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The sequence for the fusion construct (referred to as Ra12-P501S-C) was confirmed.

25 The Ra12-P501S-C fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, as described above. A small amount of protein was detected by Western blot, with some molecular weight aggregates also being observed. Expression was also detected by Western blot when the Ra12-P501S-C fusion was used for expression in BL21CodonPlus induced by CE6 phage.

b) Expression of P501S in Baculovirus

The Bac-to-Bac baculovirus expression system (BRL Life Technologies, Inc.) was used to express P501S protein in insect cells. Full-length P501S (SEQ ID NO: 113) was amplified by PCR and cloned into the XbaI site of the donor plasmid pFastBacI. The recombinant bacmid and baculovirus were prepared according to the manufacturer's instructions. The recombinant baculovirus was amplified in Sf9 cells and the high titer viral stocks were utilized to infect High Five cells (Invitrogen) to make the recombinant protein. The identity of the full-length protein was confirmed by N-terminal sequencing of the recombinant protein and by Western blot analysis (Figure 7). Specifically, 0.6 million High Five cells in 6-well plates were infected with either the unrelated control virus BV/ECD_PD (lane 2), with recombinant baculovirus for P501S at different amounts or MOIs (lanes 4-8), or were uninfected (lane 3). Cell lysates were run on SDS-PAGE under reducing conditions and analyzed by Western blot with the anti-P501S monoclonal antibody P501S-10E3-G4D3 (prepared as described below). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

The localization of recombinant P501S in the insect cells was investigated as follows. The insect cells overexpressing P501S were fractionated into fractions of nucleus, mitochondria, membrane and cytosol. Equal amounts of protein from each fraction were analyzed by Western blot with a monoclonal antibody against P501S. Due to the scheme of fractionation, both nucleus and mitochondria fractions contain some plasma membrane components. However, the membrane fraction is basically free from mitochondria and nucleus. P501S was found to be present in all fractions that contain the membrane component, suggesting that P501S may be associated with plasma membrane of the insect cells expressing the recombinant protein.

c) Expression of P501S in mammalian cells

Full-length P501S (553AA) was cloned into various mammalian expression vectors, including pCEP4 (Invitrogen), pVR1012 (Vical, San Diego, CA) and a modified form of the retroviral vector pBMN, referred to as pBIB. Transfection of P501S/pCEP4 and P501S/pVR1012 into HEK293 fibroblasts was carried out using the Fugene transfection reagent (Boehringer Mannheim). Briefly, 2 ul of Fugene reagent was diluted into 100 ul of serum-free media and incubated at room temperature for 5-10 min. This mixture was added to 1 ug of P501S plasmid DNA, mixed briefly and incubated for 30 minutes at room temperature. The Fugene/DNA mixture

was added to cells and incubated for 24-48 hours. Expression of recombinant P501S in transfected HEK293 fibroblasts was detected by means of Western blot employing a monoclonal antibody to P501S.

Transfection of p501S/pCEP4 into CHO-K cells (American Type Culture Collection, Rockville, MD) was carried out using GenePorter transfection reagent (Gene Therapy Systems, San Diego, CA). Briefly, 15 μ l of GenePorter was diluted in 500 μ l of serum-free media and incubated at room temperature for 10 min. The GenePorter/media mixture was added to 2 μ g of plasmid DNA that was diluted in 500 μ l of serum-free media, mixed briefly and incubated for 30 min at room temperature. CHO-K cells were rinsed in PBS to remove serum proteins, and the GenePorter/DNA mix was added and incubated for 5 hours. The transfected cells were then fed an equal volume of 2x media and incubated for 24-48 hours.

FACS analysis of P501S transiently infected CHO-K cells, demonstrated surface expression of P501S. Expression was detected using rabbit polyclonal antisera raised against a P501S peptide, as described below. Flow cytometric analysis was performed using a FaCScan (Becton Dickinson), and the data were analyzed using the Cell Quest program.

EXAMPLE 18

PREPARATION AND CHARACTERIZATION OF ANTIBODIES AGAINST PROSTATE-SPECIFIC POLYPEPTIDES

a) Preparation and Characterization of Antibodies against P501S

A murine monoclonal antibody directed against the carboxy-terminus of the prostate-specific antigen P501S was prepared as follows.

A truncated fragment of P501S (amino acids 355-526 of SEQ ID NO: 113) was generated and cloned into the pET28b vector (Novagen) and expressed in *E. coli* as a thioredoxin fusion protein with a histidine tag. The trx-P501S fusion protein was purified by nickel chromatography, digested with thrombin to remove the trx fragment and further purified by an acid precipitation procedure followed by reverse phase HPLC.

Mice were immunized with truncated P501S protein. Serum bleeds from mice that potentially contained anti-P501S polyclonal sera were tested for P501S-specific reactivity using ELISA assays with purified P501S and trx-P501S proteins. Serum bleeds that appeared to react specifically with P501S were then screened for P501S reactivity by Western analysis. Mice that contained a P501S-specific antibody component were sacrificed and spleen cells were used to

generate anti-P501S antibody producing hybridomas using standard techniques. Hybridoma supernatants were tested for P501S-specific reactivity initially by ELISA, and subsequently by FACS analysis of reactivity with P501S transduced cells. Based on these results, a monoclonal hybridoma referred to as 10E3 was chosen for further subcloning. A number of subclones were generated, tested for specific reactivity to P501S using ELISA and typed for IgG isotype. The results of this analysis are shown below in Table V. Of the 16 subclones tested, the monoclonal antibody 10E3-G4-D3 was selected for further study.

Table V

Isotype analysis of murine anti-P501S monoclonal antibodies

Hybridoma clone	Isotype	Estimated [Ig] in supernatant ($\mu\text{g/ml}$)
4D11	IgG1	14.6
1G1	IgG1	0.6
4F6	IgG1	72
4H5	IgG1	13.8
4H5-E12	IgG1	10.7
4H5-EH2	IgG1	9.2
4H5-H2-A10	IgG1	10
4H5-H2-A3	IgG1	12.8
4H5-H2-A10-G6	IgG1	13.6
4H5-H2-B11	IgG1	12.3
10E3	IgG2a	3.4
10E3-D4	IgG2a	3.8
10E3-D4-G3	IgG2a	9.5
10E3-D4-G6	IgG2a	10.4
10E3-E7	IgG2a	6.5
8H12	IgG2a	0.6

The specificity of 10E3-G4-D3 for P501S was examined by FACS analysis. Specifically, cells were fixed (2% formaldehyde, 10 minutes), permeabilized (0.1% saponin, 10 minutes) and stained with 10E3-G4-D3 at 0.5 – 1 $\mu\text{g/ml}$, followed by incubation with a secondary, FITC-conjugated goat anti-mouse Ig antibody (Pharmingen, San Diego, CA). Cells were then analyzed for FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. For analysis of infected cells, B-LCL were infected with a vaccinia vector that expresses P501S. To demonstrate

specificity in these assays, B-LCL transduced with a different antigen (P703P) and uninfected B-LCL vectors were utilized. 10E3-G4-D3 was shown to bind with P501S-transduced B-LCL and also with P501S-infected B-LCL, but not with either uninfected cells or P703P-transduced cells.

To determine whether the epitope recognized by 10E3-G4-D3 was found on the surface or in an intracellular compartment of cells, B-LCL were transduced with P501S or HLA-B8 as a control antigen and either fixed and permeabilized as described above or directly stained with 10E3-G4-D3 and analyzed as above. Specific recognition of P501S by 10E3-G4-D3 was found to require permeabilization, suggesting that the epitope recognized by this antibody is intracellular.

The reactivity of 10E3-G4-D3 with the three prostate tumor cell lines Lncap, PC-3 and DU-145, which are known to express high, medium and very low levels of P501S, respectively, was examined by permeabilizing the cells and treating them as described above. Higher reactivity of 10E3-G4-D3 was seen with Lncap than with PC-3, which in turn showed higher reactivity than DU-145. These results are in agreement with the real time PCR and demonstrate that the antibody specifically recognizes P501S in these tumor cell lines and that the epitope recognized in prostate tumor cell lines is also intracellular.

Specificity of 10E3-G4-D3 for P501S was also demonstrated by Western blot analysis. Lysates from the prostate tumor cell lines Lncap, DU-145 and PC-3, from P501S-transiently transfected HEK293 cells, and from non-transfected HEK293 cells were generated. Western blot analysis of these lysates with 10E3-G4-D3 revealed a 46 kDa immunoreactive band in Lncap, PC-3 and P501S-transfected HEK cells, but not in DU-145 cells or non-transfected HEK293 cells. P501S mRNA expression is consistent with these results since semi-quantitative PCR analysis revealed that P501S mRNA is expressed in Lncap, to a lesser but detectable level in PC-3 and not at all in DU-145 cells. Bacterially expressed and purified recombinant P501S (referred to as P501SStr2) was recognized by 10E3-G4-D3 (24 kDa), as was full-length P501S that was transiently expressed in HEK293 cells using either the expression vector VR1012 or pCEP4. Although the predicted molecular weight of P501S is 60.5 kDa, both transfected and "native" P501S run at a slightly lower mobility due to its hydrophobic nature.

Immunohistochemical analysis was performed on prostate tumor and a panel of normal tissue sections (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). Tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with 10E3-G4-D3 antibody for 1 hr.

HRP-labeled anti-mouse followed by incubation with DAB chromogen was used to visualize P501S immunoreactivity. P501S was found to be highly expressed in both normal prostate and prostate tumor tissue but was not detected in any of the other tissues tested.

To identify the epitope recognized by 10E3-G4-D3, an epitope mapping approach was pursued. A series of 13 overlapping 20-21 mers (5 amino acid overlap; SEQ ID NO: 489-501) was synthesized that spanned the fragment of P501S used to generate 10E3-G4-D3. Flat bottom 96 well microtiter plates were coated with either the peptides or the P501S fragment used to immunize mice, at 1 microgram/ml for 2 hours at 37 °C. Wells were then aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature, and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified antibody 10E3-G4-D3 was added at 2 fold dilutions (1000 ng – 16 ng) in PBST and incubated for 30 minutes at room temperature. This was followed by washing 6 times with PBST and subsequently incubating with HRP-conjugated donkey anti-mouse IgG (H+L) Affinipure F(ab') fragment (Jackson ImmunoResearch, West Grove, PA) at 1:20000 for 30 minutes. Plates were then washed and incubated for 15 minutes in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 8, reactivity was seen with the peptide of SEQ ID NO: 496 (corresponding to amino acids 439-459 of P501S) and with the P501S fragment but not with the remaining peptides, demonstrating that the epitope recognized by 10E3-G4-D3 is localized to amino acids 439-459 of SEQ ID NO: 113.

In order to further evaluate the tissue specificity of P501S, multi-array immunohistochemical analysis was performed on approximately 4700 different human tissues encompassing all the major normal organs as well as neoplasias derived from these tissues. Sixty-five of these human tissue samples were of prostate origin. Tissue sections 0.6 mm in diameter were formalin-fixed and paraffin embedded. Samples were pretreated with HIER using 10 mM citrate buffer pH 6.0 and boiling for 10 min. Sections were stained with 10E3-G4-D3 and P501S immunoreactivity was visualized with HRP. All the 65 prostate tissues samples (5 normal, 55 untreated prostate tumors, 5 hormone refractory prostate tumors) were positive, showing distinct perinuclear staining. All other tissues examined were negative for P501S expression.

b) Preparation and Characterization of Antibodies against P503S

A fragment of P503S (amino acids 113-241 of SEQ ID NO: 114) was expressed and purified from bacteria essentially as described above for P501S and used to immunize both rabbits

and mice. Mouse monoclonal antibodies were isolated using standard hybridoma technology as described above. Rabbit monoclonal antibodies were isolated using Selected Lymphocyte Antibody Method (SLAM) technology at Immgenics Pharmaceuticals (Vancouver, BC, Canada). Table VI, below, lists the monoclonal antibodies that were developed against P503S.

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Table VI

Antibody	Species
20D4	Rabbit
JA1	Rabbit
1A4	Mouse
1C3	Mouse
1C9	Mouse
1D12	Mouse
2A11	Mouse
2H9	Mouse
4H7	Mouse
8A8	Mouse
8D10	Mouse
9C12	Mouse
6D12	Mouse

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 20D4 and JA1 were determined and are provided in SEQ ID NO: 502 and 503, respectively.

In order to better define the epitope binding region of each of the antibodies, a series of overlapping peptides were generated that span amino acids 109-213 of SEQ ID NO: 114. These peptides were used to epitope map the anti-P503S monoclonal antibodies by ELISA as follows.

The recombinant fragment of P503S that was employed as the immunogen was used as a positive control. Ninety-six well microtiter plates were coated with either peptide or recombinant antigen at 20 ng/well overnight at 4 °C. Plates were aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature then washed in PBS containing 0.1% Tween 20 (PBST). Purified rabbit monoclonal antibodies diluted in PBST were added to the wells and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubation with Protein-A HRP conjugate at a 1:2000 dilution for a further 30 min. Plates were washed six times in PBST and incubated with tetramethylbenzidine (TMB) substrate for a further

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15 min. The reaction was stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using at ELISA plate reader. ELISA with the mouse monoclonal antibodies was performed with supernatants from tissue culture run neat in the assay.

All of the antibodies bound to the recombinant P503S fragment, with the exception
5 of the negative control SP2 supernatant. 20D4, JA1 and 1D12 bound strictly to peptide #2101 (SEQ ID NO: 504), which corresponds to amino acids 151-169 of SEQ ID NO: 114. 1C3 bound to peptide #2102 (SEQ ID NO: 505), which corresponds to amino acids 165-184 of SEQ ID NO: 114. 9C12 bound to peptide #2099 (SEQ ID NO: 522), which corresponds to amino acids 120-139 of SEQ ID NO: 114. The other antibodies bind to regions that were not examined in these studies.

10 Subsequent to epitope mapping, the antibodies were tested by FACS analysis on a cell line that stably expressed P503S to confirm that the antibodies bind to cell surface epitopes. Cells stably transfected with a control plasmid were employed as a negative control. Cells were stained live with no fixative. 0.5 ug of anti-P503S monoclonal antibody was added and cells were incubated on ice for 30 min before being washed twice and incubated with a FITC-labelled goat
15 anti-rabbit or mouse secondary antibody for 20 min. After being washed twice, cells were analyzed with an Excalibur fluorescent activated cell sorter. The monoclonal antibodies 1C3, 1D12, 9C12, 20D4 and JA1, but not 8D3, were found to bind to a cell surface epitope of P503S.

In order to determine which tissues express P503S, immunohistochemical analysis was performed, essentially as described above, on a panel of normal tissues (prostate, adrenal,
20 breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). HRP-labeled anti-mouse or anti-rabbit antibody followed by incubation with TMB was used to visualize P503S immunoreactivity. P503S was found to be highly expressed in prostate tissue, with lower levels of expression being observed in cervix, colon, ileum and kidney, and no expression being observed in adrenal, breast, duodenum, gall bladder, ovary,
25 pancreas, parotid gland, skeletal muscle, spleen and testis.

Western blot analysis was used to characterize anti-P503S monoclonal antibody specificity. SDS-PAGE was performed on recombinant (rec) P503S expressed in and purified from bacteria and on lysates from HEK293 cells transfected with full length P503S. Protein was transferred to nitrocellulose and then Western blotted with each of the anti-P503S monoclonal
30 antibodies (20D4, JA1, 1D12, 6D12 and 9C12) at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to either a goat anti-mouse monoclonal antibody or to protein A-sepharose. The monoclonal antibody 20D4 detected the

appropriate molecular weight 14 kDa recombinant P503S (amino acids 113-241) and the 23.5 kDa species in the HEK293 cell lysates transfected with full length P503S. Other anti-P503S monoclonal antibodies displayed similar specificity by Western blot.

5 **c) Preparation and Characterization of Antibodies against P703P**

Rabbits were immunized with either a truncated (P703Ptrl; SEQ ID NO: 172) or full-length mature form (P703Pfl; SEQ ID NO: 523) of recombinant P703P protein was expressed in and purified from bacteria as described above. Affinity purified polyclonal antibody was generated using immunogen P703Pfl or P703Ptrl attached to a solid support. Rabbit monoclonal
10 antibodies were isolated using SLAM technology at Immgenics Pharmaceuticals. Table VII below lists both the polyclonal and monoclonal antibodies that were generated against P703P.

Table VII

Antibody	Immunogen	Species/type
Aff. Purif. P703P (truncated); #2594	P703Ptrl	Rabbit polyclonal
Aff. Purif. P703P (full length); #9245	P703Pfl	Rabbit polyclonal
2D4	P703Ptrl	Rabbit monoclonal
8H2	P703Ptrl	Rabbit monoclonal
7H8	P703Ptrl	Rabbit monoclonal

15

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 8H2, 7H8 and 2D4 were determined and are provided in SEQ ID NO: 506-508, respectively.

Epitope mapping studies were performed as described above. Monoclonal
20 antibodies 2D4 and 7H8 were found to specifically bind to the peptides of SEQ ID NO: 509 (corresponding to amino acids 145-159 of SEQ ID NO: 172) and SEQ ID NO: 510 (corresponding to amino acids 11-25 of SEQ ID NO: 172), respectively. The polyclonal antibody 2594 was found to bind to the peptides of SEQ ID NO: 511-514, with the polyclonal antibody 9427 binding to the peptides of SEQ ID NO: 515-517.

25 The specificity of the anti-P703P antibodies was determined by Western blot analysis as follows. SDS-PAGE was performed on (1) bacterially expressed recombinant antigen; (2) lysates of HEK293 cells and Ltk-/- cells either untransfected or transfected with a plasmid

expressing full length P703P; and (3) supernatant isolated from these cell cultures. Protein was transferred to nitrocellulose and then Western blotted using the anti-P703P polyclonal antibody #2594 at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to an anti-rabbit antibody. A 35 kDa immunoreactive band could be observed with recombinant P703P. Recombinant P703P runs at a slightly higher molecular weight since it is epitope tagged. In lysates and supernatants from cells transfected with full length P703P, a 30 kDa band corresponding to P703P was observed. To assure specificity, lysates from HEK293 cells stably transfected with a control plasmid were also tested and were negative for P703P expression. Other anti-P703P antibodies showed similar results.

Immunohistochemical studies were performed as described above, using anti-P703P monoclonal antibody. P703P was found to be expressed at high levels in normal prostate and prostate tumor tissue but was not detectable in all other tissues tested (breast tumor, lung tumor and normal kidney).

EXAMPLE 19

CHARACTERIZATION OF CELL SURFACE EXPRESSION AND CHROMOSOME LOCALIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

This example describes studies demonstrating that the prostate-specific antigen P501S is expressed on the surface of cells, together with studies to determine the probable chromosomal location of P501S.

The protein P501S (SEQ ID NO: 113) is predicted to have 11 transmembrane domains. Based on the discovery that the epitope recognized by the anti-P501S monoclonal antibody 10E3-G4-D3 (described above in Example 17) is intracellular, it was predicted that following transmembrane determinants would allow the prediction of extracellular domains of P501S. Fig. 9 is a schematic representation of the P501S protein showing the predicted location of the transmembrane domains and the intracellular epitope described in Example 17. Underlined sequence represents the predicted transmembrane domains, bold sequence represents the predicted extracellular domains, and italicized sequence represents the predicted intracellular domains. Sequence that is both bold and underlined represents sequence employed to generate polyclonal rabbit serum. The location of the transmembrane domains was predicted using HHMTOP as

described by Tusnady and Simon (Principles Governing Amino Acid Composition of Integral Membrane Proteins: Applications to Topology Prediction, *J. Mol. Biol.* 283:489-506, 1998).

Based on Fig. 9, the P501S domain flanked by the transmembrane domains corresponding to amino acids 274-295 and 323-342 is predicted to be extracellular. The peptide of SEQ ID NO: 518 corresponds to amino acids 306-320 of P501S and lies in the predicted extracellular domain. The peptide of SEQ ID NO: 519, which is identical to the peptide of SEQ ID NO: 518 with the exception of the substitution of the histidine with an asparagine, was synthesized as described above. A Cys-Gly was added to the C-terminus of the peptide to facilitate conjugation to the carrier protein. Cleavage of the peptide from the solid support was carried out using the following cleavage mixture: trifluoroacetic acid:ethanediol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for two hours, the peptide was precipitated in cold ether. The peptide pellet was then dissolved in 10% v/v acetic acid and lyophilized prior to purification by C18 reverse phase hplc. A gradient of 5-60% acetonitrile (containing 0.05% TFA) in water (containing 0.05% TFA) was used to elute the peptide. The purity of the peptide was verified by hplc and mass spectrometry, and was determined to be >95%. The purified peptide was used to generate rabbit polyclonal antisera as described above.

Surface expression of P501S was examined by FACS analysis. Cells were stained with the polyclonal anti-P501S peptide serum at 10 µg/ml, washed, incubated with a secondary FITC-conjugated goat anti-rabbit Ig antibody (ICN), washed and analyzed for FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. To demonstrate specificity in these assays, B-LCL transduced with an irrelevant antigen (P703P) or nontransduced were stained in parallel. For FACS analysis of prostate tumor cell lines, Lncap, PC-3 and DU-145 were utilized. Prostate tumor cell lines were dissociated from tissue culture plates using cell dissociation medium and stained as above. All samples were treated with propidium iodide (PI) prior to FACS analysis, and data was obtained from PI-excluding (i.e. intact and non-permeabilized) cells. The rabbit polyclonal serum generated against the peptide of SEQ ID NO: 519 was shown to specifically recognize the surface of cells transduced to express P501S, demonstrating that the epitope recognized by the polyclonal serum is extracellular.

To determine biochemically if P501S is expressed on the cell surface, peripheral membranes from Lncap cells were isolated and subjected to Western blot analysis. Specifically, Lncap cells were lysed using a dounce homogenizer in 5 ml of homogenization buffer (250 mM

sucrose, 10 mM HEPES, 1mM EDTA, pH 8.0, 1 complete protease inhibitor tablet (Boehringer Mannheim)). Lysate samples were spun at 1000 g for 5 min at 4 °C. The supernatant was then spun at 8000g for 10 min at 4 °C. Supernatant from the 8000g spin was recovered and subjected to a 100,000g spin for 30 min at 4 °C to recover peripheral membrane. Samples were then separated by SDS-PAGE and Western blotted with the mouse monoclonal antibody 10E3-G4-D3 (described above in Example 17) using conditions described above. Recombinant purified P501S, as well as HEK293 cells transfected with and over-expressing P501S were included as positive controls for P501S detection. LCL cell lysate was included as a negative control. P501S could be detected in Lncap total cell lysate, the 8000g (internal membrane) fraction and also in the 100,000g (plasma membrane) fraction. These results indicate that P501S is expressed at, and localizes to, the peripheral membrane.

To demonstrate that the rabbit polyclonal antiserum generated to the peptide of SEQ ID NO: 519 specifically recognizes this peptide as well as the corresponding native peptide of SEQ ID NO: 518, ELISA analyses were performed. For these analyses, flat-bottomed 96 well microtiter plates were coated with either the peptide of SEQ ID NO: 519, the longer peptide of SEQ ID NO: 520 that spans the entire predicted extracellular domain, the peptide of SEQ ID NO: 521 which represents the epitope recognized by the P501S-specific antibody 10E3-G4-D3, or a P501S fragment (corresponding to amino acids 355-526 of SEQ ID NO: 113) that does not include the immunizing peptide sequence, at 1 µg/ml for 2 hours at 37 °C. Wells were aspirated, blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified anti-P501S polyclonal rabbit serum was added at 2 fold dilutions (1000 ng - 125 ng) in PBST and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubating with HRP-conjugated goat anti-rabbit IgG (H+L) Affinipure F(ab') fragment at 1:20000 for 30 min. Plates were then washed and incubated for 15 min in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 11, the anti-P501S polyclonal rabbit serum specifically recognized the peptide of SEQ ID NO: 519 used in the immunization as well as the longer peptide of SEQ ID NO: 520, but did not recognize the irrelevant P501S-derived peptides and fragments.

In further studies, rabbits were immunized with peptides derived from the P501S sequence and predicted to be either extracellular or intracellular, as shown in Fig. 9. Polyclonal rabbit sera were isolated and polyclonal antibodies in the serum were purified, as described above.

To determine specific reactivity with P501S, FACS analysis was employed, utilizing either B-LCL transduced with P501S or the irrelevant antigen P703P, of B-LCL infected with vaccinia virus-expressing P501S. For surface expression, dead and non-intact cells were excluded from the analysis as described above. For intracellular staining, cells were fixed and permeabilized as described above. Rabbit polyclonal serum generated against the peptide of SEQ ID NO: 548, which corresponds to amino acids 181-198 of P501S, was found to recognize a surface epitope of P501S. Rabbit polyclonal serum generated against the peptide SEQ ID NO: 551, which corresponds to amino acids 543-553 of P501S, was found to recognize an epitope that was either potentially extracellular or intracellular since in different experiments intact or permeabilized cells were recognized by the polyclonal sera. Based on similar deductive reasoning, the sequences of SEQ ID NO: 541-547, 549 and 550, which correspond to amino acids 109-122, 539-553, 509-520, 37-54, 342-359, 295-323, 217-274, 143-160 and 75-88, respectively, of P501S, can be considered to be potential surface epitopes of P501S recognized by antibodies.

The chromosomal location of P501S was determined using the GeneBridge 4 Radiation Hybrid panel (Research Genetics). The PCR primers of SEQ ID NO: 528 and 529 were employed in PCR with DNA pools from the hybrid panel according to the manufacturer's directions. After 38 cycles of amplification, the reaction products were separated on a 1.2% agarose gel, and the results were analyzed through the Whitehead Institute/MIT Center for Genome Research web server (<http://www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl>) to determine the probable chromosomal location. Using this approach, P501S was mapped to the long arm of chromosome 1 at WI-9641 between q32 and q42. This region of chromosome 1 has been linked to prostate cancer susceptibility in hereditary prostate cancer (Smith *et al. Science* 274:1371-1374, 1996 and Berthon *et al. Am. J. Hum. Genet.* 62:1416-1424, 1998). These results suggest that P501S may play a role in prostate cancer malignancy.

From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for the purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the present invention is not limited except as by the appended claims.

CLAIMS

1. An isolated polypeptide comprising at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536;

(b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and

(c) complements of any of the sequence of (a) or (b).

2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID No: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotide sequences.

3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 108, 112, 113, 114, 172, 176, 178, 327, 329, 331, 339, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534 and 537-550.

4. An isolated polynucleotide encoding at least 15 contiguous amino acid residues of a prostate-specific protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the protein
5 comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413,
10 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing sequences.

5. An isolated polynucleotide encoding a prostate-specific protein, or a
15 variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396,
20 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing sequences.

6. An isolated polynucleotide comprising a sequence recited in any one
25 of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530,
30 531, 533, 535 and 536.

7. An isolated polynucleotide comprising a sequence that hybridizes under moderately stringent conditions to a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536.

8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

9. An expression vector comprising a polynucleotide according to any one of claims 4-8.

10. A host cell transformed or transfected with an expression vector according to claim 9.

11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a prostate-specific protein, the protein comprising an amino acid sequence encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536 or a complement of any of the foregoing polynucleotide sequences.

12. A monoclonal antibody that specifically binds to an amino acid sequence selected from the group consisting of SEQ ID NO: 496, 504, 505, 509-517, 519, 520, 522 and 539-551.
- 5 13. A monoclonal antibody comprising a complementarity determining region selected from the group consisting of SEQ ID NO: 502, 503 and 506-508.
- 10 14. A fusion protein comprising at least one polypeptide according to claim 1.
- 15 15. A fusion protein according to claim 14, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.
- 16 16. A fusion protein according to claim 14, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.
- 20 17. A fusion protein according to claim 14, wherein the fusion protein comprises an affinity tag.
18. An isolated polynucleotide encoding a fusion protein according to claim 14.
- 25 19.. A pharmaceutical composition comprising a physiologically acceptable carrier and at least one component selected from the group consisting of:
- (a) a polypeptide according to claim 1;
 - (b) a polynucleotide according to claim 4;
 - (c) an antibody according to any one of claims 11-13;
 - 30 (d) a fusion protein according to claim 14; and

(e) a polynucleotide according to claim 18.

20. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

- 5 (a) a polypeptide according to claim 1;
(b) a polynucleotide according to claim 4;
(c) an antibody according to any one of claims 11-13;
(d) a fusion protein according to claim 14; and
(e) a polynucleotide according to claim 18.

10

21. A vaccine according to claim 20, wherein the immunostimulant is an adjuvant.

22. A vaccine according to claim 20, wherein the immunostimulant
15 induces a predominantly Type I response.

23. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 19.

20

24. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 20.

25. A pharmaceutical composition comprising an antigen-presenting cell
25 that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

26. A pharmaceutical composition according to claim 25, wherein the antigen presenting cell is a dendritic cell or a macrophage.

27. A vaccine comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with an immunostimulant.
- 5 28. A vaccine according to claim 27, wherein the immunostimulant is an adjuvant.
29. A vaccine according to claim 27, wherein the immunostimulant induces a predominantly Type I response.
- 10 30. A vaccine according to claim 27, wherein the antigen-presenting cell is a dendritic cell.
31. A method for inhibiting the development of a cancer in a patient, 15 comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide encoded by a polynucleotide recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, and thereby inhibiting the development of a cancer in the patient.
- 20 32. A method according to claim 31, wherein the antigen-presenting cell is a dendritic cell.
33. A method according to any one of claims 23, 24 and 31, wherein the 25 cancer is prostate cancer.
34. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate-specific protein, wherein the protein comprises an amino acid sequence that is 30 encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536; and

(ii) complements of the foregoing polynucleotides;

5 wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the prostate-specific protein from the sample.

35. A method according to claim 34, wherein the biological sample is
10 blood or a fraction thereof.

36. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 50.

15

37. A method for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with at least one component selected from the group consisting of:

(i) a polypeptide according to claim 1;

20 (ii) a polypeptide encoded by a polynucleotide comprising a sequence provided in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;

(iii) a polynucleotide encoding a polypeptide of (i) or (ii); and

(iv) an antigen presenting cell that expresses a polypeptide of (i) or (ii),

25 under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

38. An isolated T cell population, comprising T cells prepared according to the method of claim 37.

30

39. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 38.

5 40. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

(i) a polypeptide according to claim 1;

10 (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;

(iii) a polynucleotide encoding a polypeptide of (i) or (ii); or

15 (iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

20 41. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

25 (i) a polypeptide according to claim 1;

(ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;

30 (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or

(iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate;

(b) cloning at least one proliferated cell to provide cloned T cells; and

5 (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

42. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

10 (a) contacting a biological sample obtained from a patient with a binding agent that binds to a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-111,
15 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536; and

(ii) complements of the foregoing polynucleotides;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent; and

20 (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

43. A method according to claim 42, wherein the binding agent is an antibody.

25

44. A method according to claim 43, wherein the antibody is a monoclonal antibody.

45. A method according to claim 42, wherein the cancer is prostate
30 cancer.

46. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

- 5 (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;
- 10 (b) detecting in the sample an amount of polypeptide that binds to the binding agent;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polypeptide detected in step (c) to the
15 amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

47. A method according to claim 46, wherein the binding agent is an antibody.

20

48. A method according to claim 47, wherein the antibody is a monoclonal antibody.

49. A method according to claim 46, wherein the cancer is a prostate
25 cancer.

50. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

- (a) contacting a biological sample obtained from a patient with an
30 oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein,

wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;

5 (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

(c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

10

51. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

15

52. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

53. A method for monitoring the progression of a cancer in a patient,
20 comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315,
25 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained from
30 the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

5 54. A method according to claim 53, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

 55. A method according to claim 53, wherein the amount of
10 polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

 56. A diagnostic kit, comprising:
 (a) one or more antibodies according to claim 11; and
15 (b) a detection reagent comprising a reporter group.

 57. A kit according to claim 56, wherein the antibodies are immobilized on a solid support.

20 58. A kit according to claim 56, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

 59. A kit according to claim 56, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups,
25 enzymes, biotin and dye particles.

 60. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is
30 encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45,

47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 5 452, 453, 459-461, 468-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides.

61. A oligonucleotide according to claim 60, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NO: 10 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-476, 524, 526, 530, 531, 533, 535 and 536.

15

62. A diagnostic kit, comprising:

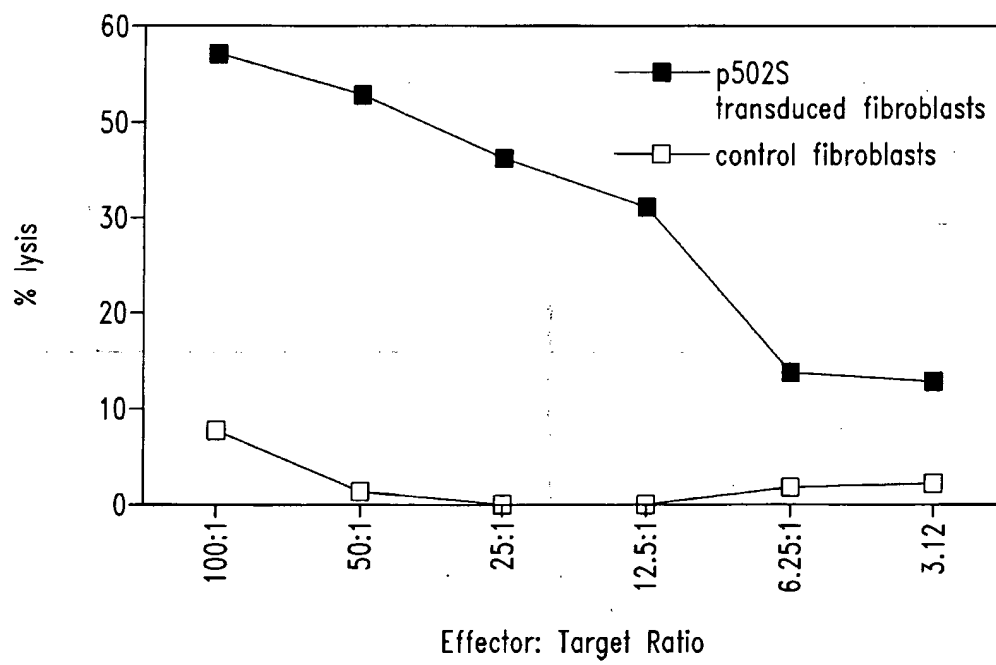
(a) an oligonucleotide according to claim 61; and

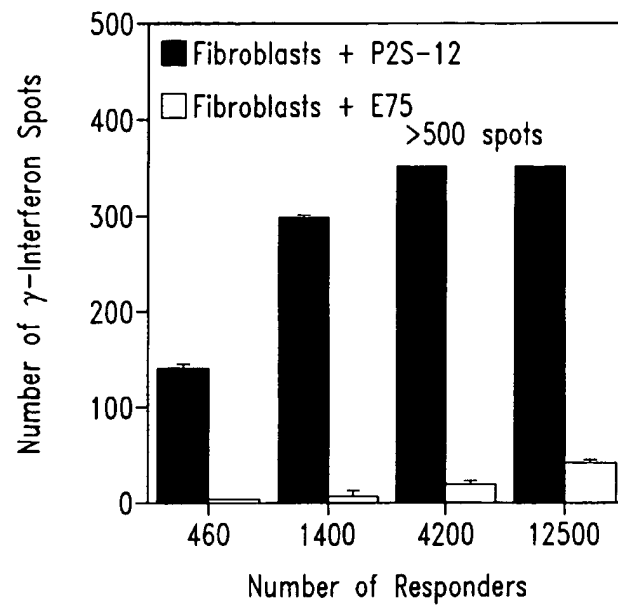
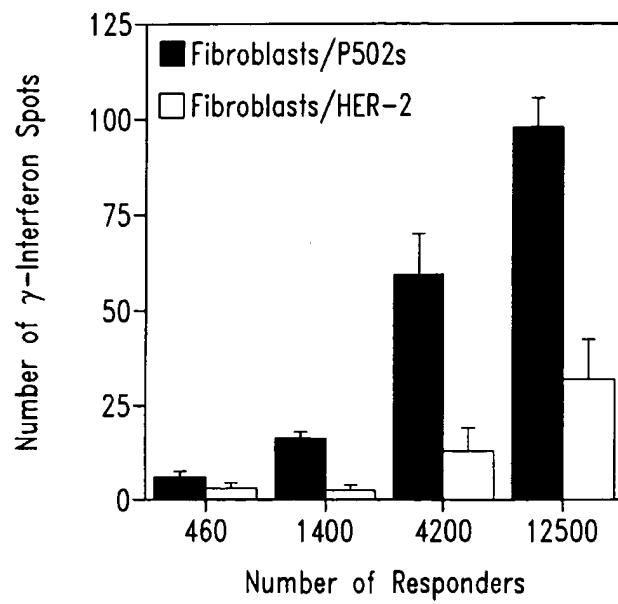
(b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

20

63. A host cell according to claim 10, wherein the cell is selected from the group consisting of: *E. coli*, baculovirus and mammalian cells.

64. A recombinant protein produced by a host cell according to claim 25 10.

*Fig. 1*

*Fig. 2A**Fig. 2B*

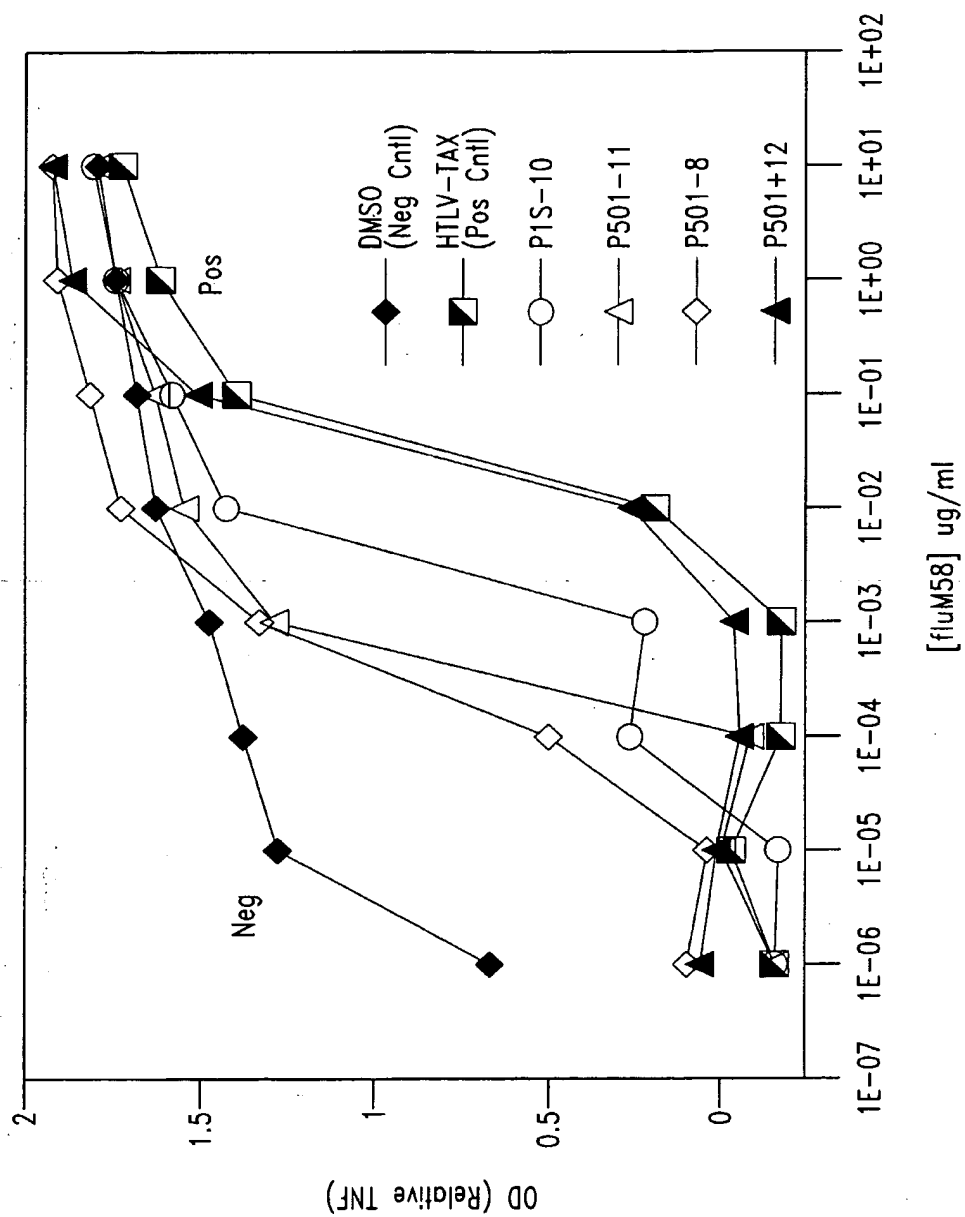
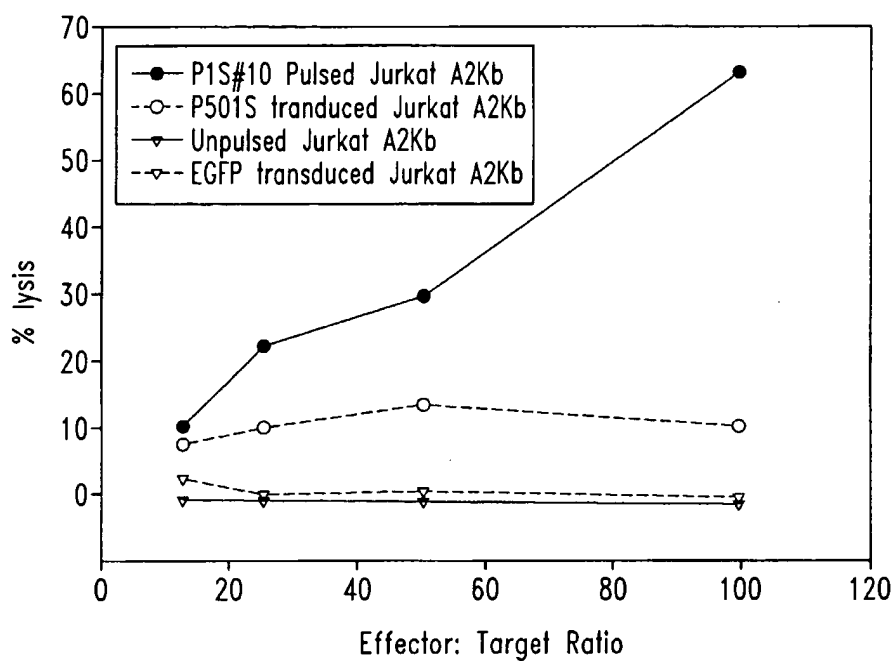
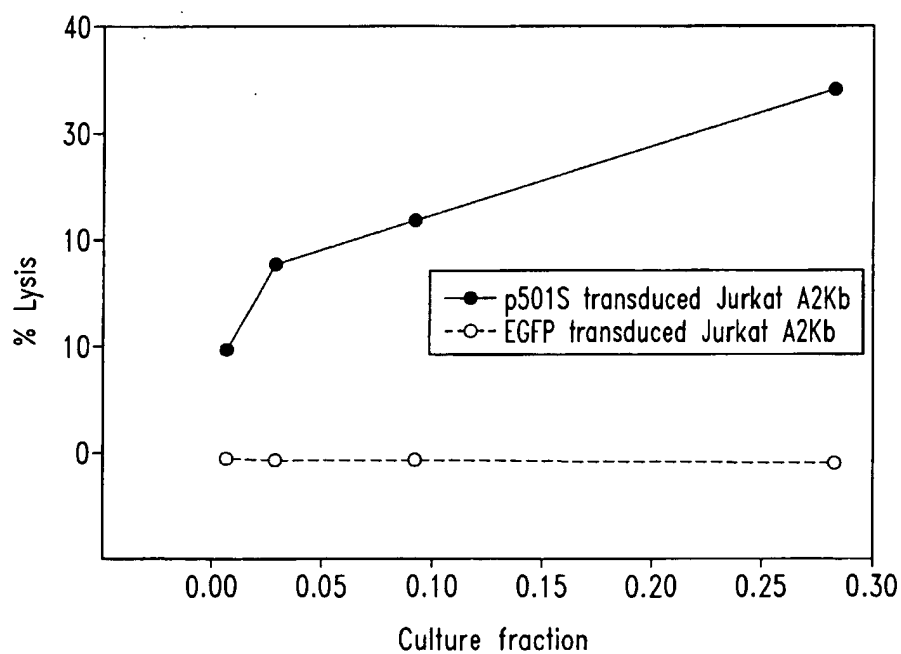
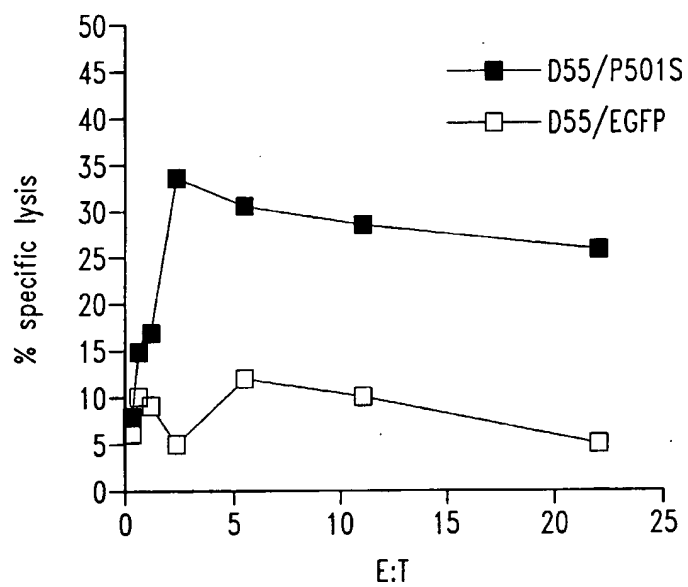
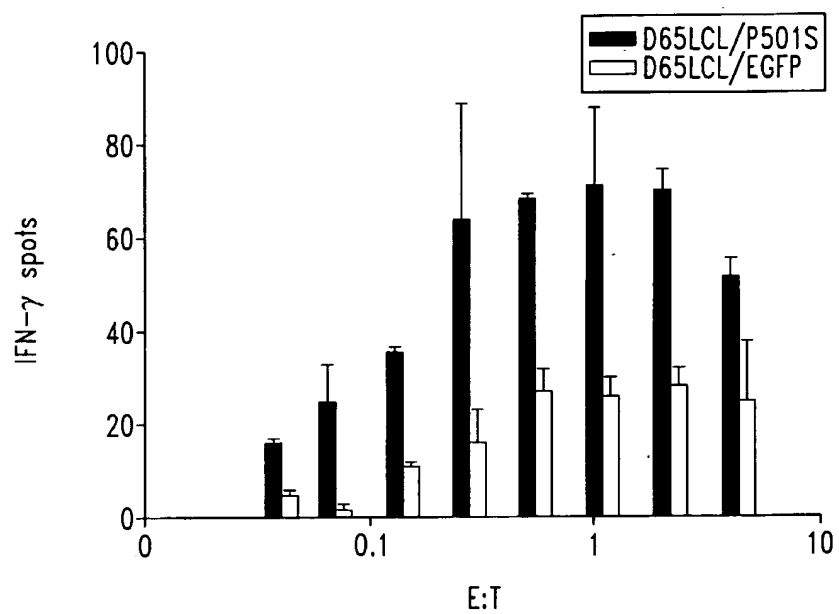
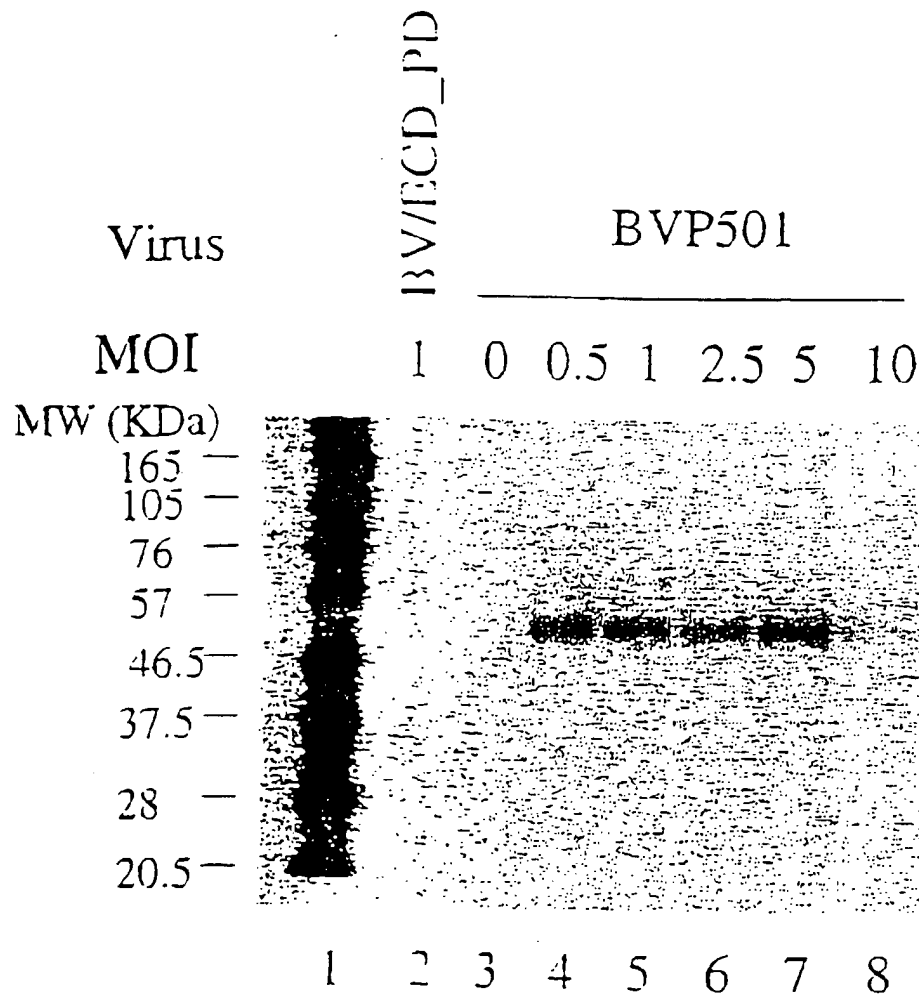


Fig. 3

*Fig. 4**Fig. 5*

*Fig. 6A**Fig. 6B*

Expression of P501S by the Baculovirus Expression System



0.6 million high 5 cells in 8-well plate were infected with an unrelated control virus BV/ECD_PD (lane 2), without virus (lane 3), or with recombinant baculovirus for P501 at different MOIs (lane 4 - 8). Cell lysates were run on SDS-PAGE under the reducing conditions and analyzed by Western blot with a monoclonal antibody against P501S (P501S-10E3-G4D3). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

Fig. 7

Schematic of P501S with predicted
transmembrane, cytoplasmic, and extracellular regions

MVQRLWVSRLLRHRK AQLLLVNLLTFGLEVCLAAGIT **YVPPLLLEVGVEEKFM**
TMVLGIGPVLGLVCYPLLGSAS
 DHWRGRYGRRRP FIWALSLGILLSLFLIPRAGWL **AGLLCPDPRPLE** LALLILGVGLLDFCGQVCFTPL
EALLSDLFRDPDHCRQ AYSVYAFMISLGGCLGYLLPAI **DWDT**SALAPYLG**TQEE**
CLFGLLTLIFLTCVAATLLV AEAAALGPTEPAEGLSAPSLSPHCCPCRARLAFRNLGALLPRL
HQLCCRMPTLRR LFVAELCSWMALMTFTLFYTDF **VGEGLYQGV**PRAEPGTEARRHYDEGVR
MGSLGLFLQCAISLVFSLVM DRLVQRFGTRAVYLAS VAAFPVAAGATCLSHSVAVVTA **SAA**
LTGFTFSALQILPYTLASLY HREKQVFLPKYRGDTGGASSEDSLMTSFLPGPKPGAPFPNGHVGAGGSGL
LPPPPALCGASACDVSVRVVVGEPTEARVVPGRG ICLDLAILDSAFLLSQVAPSLF **MGSIVQLSQS**
VTAYMVSAAGLGLVAIYFAT QVVFDKSDLAKYSA

Underlined sequence: Predicted transmembrane domain; **Bold sequence**:
 Predicted extracellular domain; *Italic sequence*: Predicted intracellular
 domain. Sequence in bold/underlined: used generate polyclonal rabbit
 serum

Localization of domains predicted using HMMTOP (G.E. Tusnady and I. Simon
 (1998) Principles Governing Amino Acid Composition of Integral Membrane
 Proteins: Applications to topology Prediction. J. Mol Biol. 283, 489-506.

Fig. 9

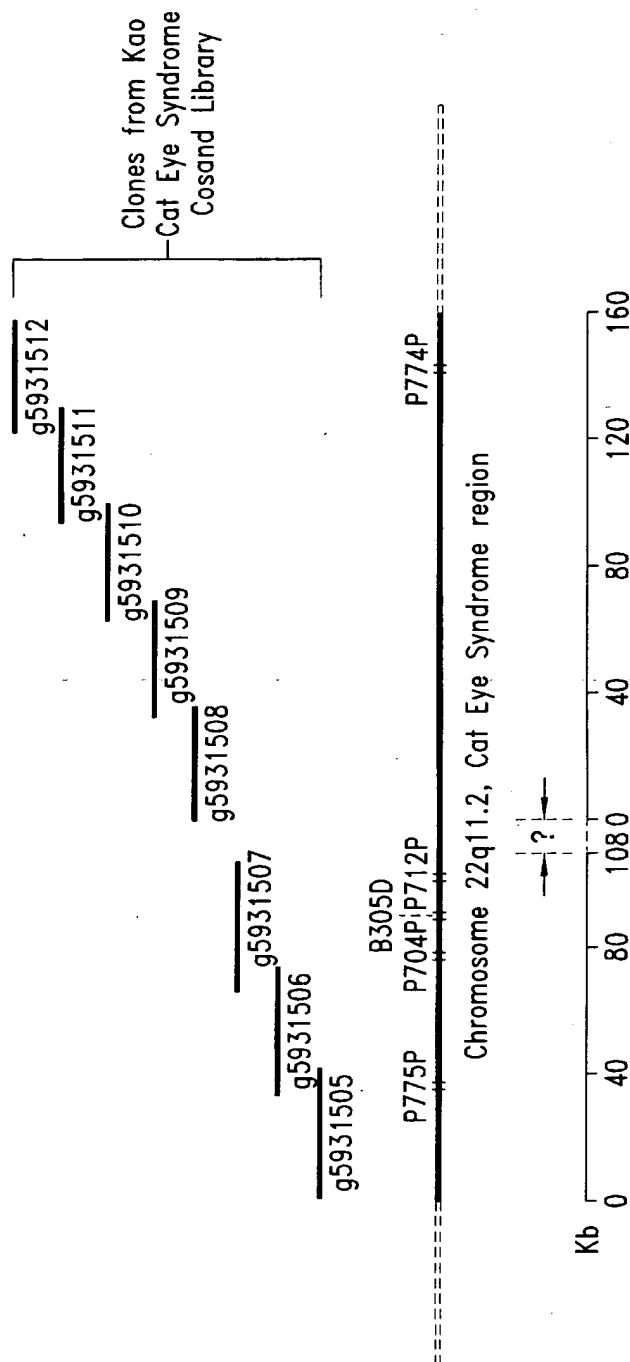


Fig. 10

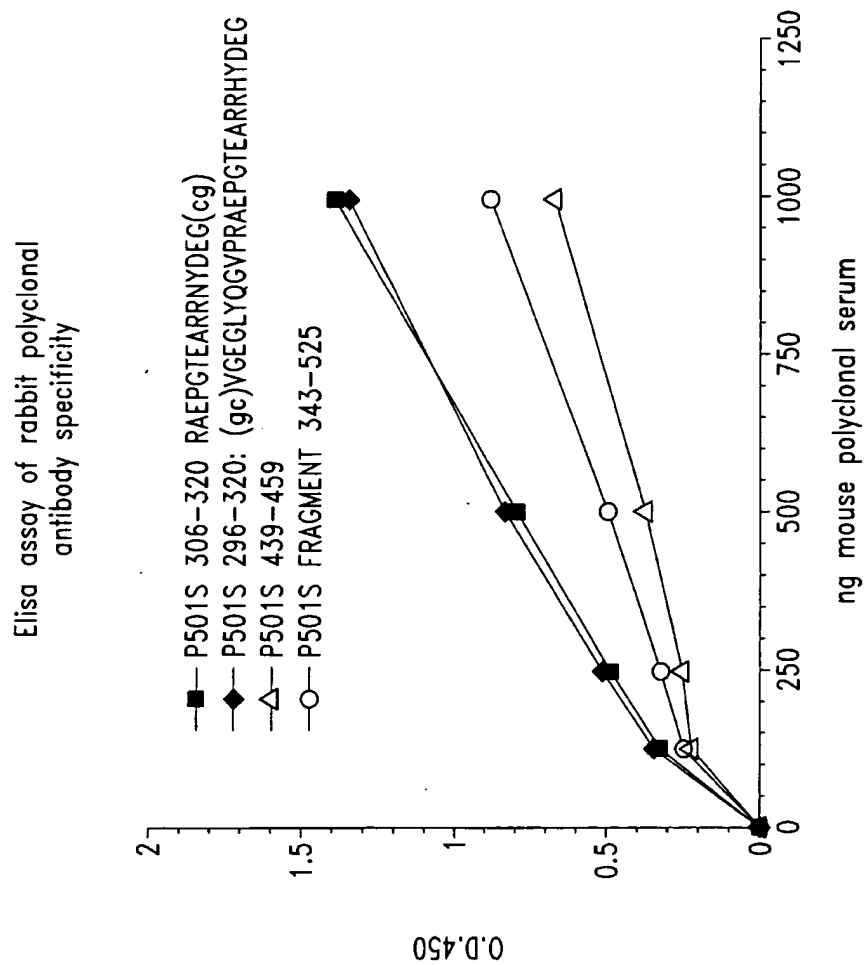


Fig. 11

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 Harlocker, Susan Louise
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 Reed, Steven G.
 Kalos, Michael
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 Solk, John
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<120> COMPOSITIONS AND METHODS FOR THE THERAPY AND
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ttentaccgc	cgnatntgtc	ccanctgttt	cngtgccnac	tccancttct	nggacgtgcg	420
ctacatacgc	cggantcnc	ntccccgctt	tgccctatc	cacgtncan	caacaaattt	480
cncntantg	caccnattec	caenttttnc	agntttccnc	nncngcttc	cttntaaaag	540
ggttganccc	cggaaaatnc	cccaaagggg	gggggcccng	tacccaactn	ccccctnata	600
gctgaantcc	ccatnaccnn	gnctcnatgg	ancntccnt	tttaannacn	ttctnaactt	660
gggaanance	ctcgnccntn	cccccttaa	tccnccttg	cnangnncnt	cccccnntcc	720
ncccnntng	gcntntnann	cnaaaaaggc	ccnnancaa	tctcctnnn	cctcanttcg	780
ccanccctcg	aaatcgccn	c				801

<210> 10

<211> 789

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(789)

<223> n = A,T,C or G

<400> 10

cagtctatnt	ggccagtgtg	gcagctttcc	ctgtggtg	cggtgccaca	tgctgtccc	60
acagtgtggc	cgtggtgaca	gcttcagccg	ccctcacccg	gttcaccttc	tcagccctgc	120
agatcctgcc	ctacacactg	gcctccctct	accaccggga	gaagcaggtg	ttcctgccc	180
aataccgagg	ggacactgga	ggtgctagca	gtgaggacag	cctgatgacc	agcttctg	240
caggccctaa	gcctggagct	cccttcccta	atggacacgt	gggtgctgga	ggcagtggcc	300
tgctcccacc	tccacccgcg	ctctgcgggg	cctctgctg	tgatgtctcc	gtacgtgtgg	360
tgggtgggtga	gccaccgan	gccaggggtg	ttccgggccc	gggcactctg	ctggacctcg	420
ccatcctgga	tagtgcttcc	tgctgtccca	ngtggcccca	tccctgttta	tgggctccat	480
tgtccagctc	agccagtctg	tactgccta	tatggtgtct	gccgcaggcc	tgggtctggt	540
ccatttact	ttgtacaca	ggtantattt	gacaagaacg	anttggccaa	atactcagcg	600
ttaaaaaatt	ccagcaacat	tgggggtgga	aggcctgcct	cactgggtcc	aactccccgc	660
tcctgttaac	cccatggggc	tgcgggcttg	gccgccaat	tctgttctg	ccaaantnat	720
gtggtctct	gctgccacct	gttctgtggt	gaagtgcnta	cngcncanct	nggggggtng	780
ggngttccc						789

<210> 11

<211> 772

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(772)

<223> n = A,T,C or G

<400> 11

```

cccaccctac ccaaataatta gacaccaaca cagaaaagct agcaatggat tcccttctac      60
tttggttaaat aaataagtta aatattttaa tgcctgtgtc tctgtgatgg caacagaagg      120
accaacaggc cacatcctga taaaaggtaa gaggggggtg gatcagcaaa aagacagtgc      180
tgtgggctga ggggacctgg ttcttgtgtg ttgcccctca ggactcttcc cctacaaata      240
actttcatat gttcaaatcc catggaggag tgtttcatcc tagaaactcc catgcaagag      300
ctacattaaa cgaagctgca ggttaagggg cttanagatg ggaaaccagg tgactgagtt      360
tattcagctc caaaaaacc ttctctaggt gtgtctcaac taggaggcta gctgttaacc      420
ctgagcctgg gtaatccacc tgcagagtcc ccgcattcca gtgcatggaa cccttctggc      480
ctccctgtat aagtccagac tgaaccccc ttggaaggnc tccagtcagg cagccctana      540
aactggggaa aaaagaaaag gacgccccan cccccagctg tgcanctacg cacctcaaca      600
gcacaggggtg gcagcaaaaa aaccacttta ctttggcaca aacaaaaact nggggggggca      660
accccgccac ccnangggg gttaacagga ancngggnaa cntggaaccc aattnaggca      720
ggcccnccac ccnaatntt gctgggaaat ttttctctcc ctaaattntt tc              772

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<210> 12

<211> 751

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(751)

<223> n = A,T,C or G

<400> 12

```

gccccaatte cagctgccac accaccacag gtgactgcat tagttcggat gtcatacaaa      60
agctgattga agcaaccctc tactttttgg tegtgagcct tttgcttggg gcagggtttca      120
ttggctgtgt tggtgacgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg      180
aagtanggtg agtctcaaaa atccgtatag ttggtgaagc cacagcactt gagccctttc      240
atggtgggtg tccacacttg agtgaagtct tcttggaac cataatcttt cttgatggca      300
ggcactacca gcaacgtcag ggaagtgtc agccattgtg gtgtacacca aggcgaccac      360
agcagctgcn acctcagcaa tgaagatgan gaggangatg aagaagaacg tcncgagggc      420
acacttgctc tcagtcttan caccatanca gcccntgaaa accaananca aagaccacna      480
cnccggctgc gatgaagaaa tnacccncg ttgacaaact tgcattggcag tggganccac      540
agtggccnna aaaatcttca aaaaggatgc cccatcnatt gaccccccaa atgcccactg      600
ccaacagggg ctgccccacn cncnnaacga tgancnatt gnacaagatc tncntggtct      660
tnatnaacnt gaacctgcn tngtggtctc tgttcaggnc cnnggcctga cttctnaann      720
aangaactcn gaagncceca cngganannc g                                751

```

<210> 13

<211> 729

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(729)

<223> n = A,T,C or G

<400> 13

gagccaggcg	tcctctgcc	tgccactca	gtggcaaac	ccgggagctg	ttttgtcctt	60
tgtggancct	cagcagtncc	ctctttcaga	actcantgcc	aagancctg	aacaggagcc	120
accatgcagt	gcttcagctt	cattaagacc	atgatgatcc	tcttcaattt	gctcatcttt	180
ctgtgtggtg	cagccctggt	ggcagtgggc	atctgggtgt	caatcgatgg	ggcatccttt	240
ctgaagatct	tcgggccact	gtcgtccagt	gccatgcagt	ttgtcaacgt	gggctacttc	300
ctcatgcag	ccggcggtgt	ggtcttagct	ctagggttcc	tgggctgcta	tgggtgctaag	360
actgagagca	agtgtgccct	cgtgacgttc	ttcttcatcc	tcctcctcat	cttcattgct	420
gaggttgcaa	tgtgtgggtc	gccttggtgt	acaccacaat	ggctgagcac	ttcctgacgt	480
tgtgtgtaat	gcctgccatc	aanaaaagat	tatgggttcc	caggaanact	tcactcaagt	540
gttgaacac	caccatgaaa	gggtcgaagt	gctgtggctt	cnnccaacta	tacggatttt	600
gaagantcac	ctacttcaaa	gaaaanagt	cctttccccc	atttctgttg	caattgacaa	660
acgtcccaa	cacagccaat	tgaaaacctg	cacccaaccc	aaanggggtcc	ccaaccanaa	720
attnaagg						729

<210> 14

<211> 816

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (816)

<223> n = A,T,C or G

<400> 14

tgtcttctct	caaagttggt	cttgttgcca	taacaaccac	cataggtaaa	gcgggagcag	60
tgttcgctga	aggggttgta	gtaccagcgc	gggatgctct	ccttgacagag	tcctgtgtct	120
ggcaggtcca	cgcagtgcgc	tttgtcactg	gggaaatgga	tgcgctggag	ctcgtcaaag	180
ccactcgtgt	atttttcaca	ggcagcctcg	tcgacgcgt	cggggcagtt	gggggtgtct	240
tcacactcca	ggaaactgtc	natgcagcag	ccattgctgc	agcggaaactg	ggtgggctga	300
cangtgccag	agcacactgg	atggcgctct	tccatgnnan	gggccctgng	ggaaagtccc	360
tgancccan	anctgcctct	caaangcccc	accttgacac	ccccgacagg	ctagaatgga	420
atcttcttcc	cgaaggttag	ttnttcttgt	tgcccaancc	ancccntaa	acaaactctt	480
gcanatctgc	tcgnggggg	tctantacc	ancgtgggaa	aagaacccca	ggcngcgaac	540
caancttggt	tggatnoga	gnataatct	ncntttctgc	ttggtggaca	gcaccantna	600
ctgtnnanct	ttagnccntg	gtcctcntgg	gttgnncttg	aacctaatcn	ccnntcaact	660
gggacaaggt	aantngccnt	cctttnaatt	cccnancntn	ccccctggtt	tgggggtttt	720
cncnctcta	ccccagaaan	ncctgttctc	cccccaacta	ggggccnaaa	ccnnttnttc	780
cacaacctn	ccccaccac	gggttcngnt	ggttng			816

<210> 15

<211> 783

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (783)

<223> n = A,T,C or G

<400> 15

ccaaggcctg	ggcaggcata	nacttgaagg	tacaacccca	ggaaccctg	gtgctgaagg	60
atgtggaaaa	cacagattgg	cgcctactgc	gggggtgacac	ggatgtcagg	gtagagagga	120
aagacccaaa	ccaggtggaa	ctgtggggac	tcaaggaang	cacctacctg	ttccagctga	180
cagtgaactag	ctcagaccac	ccagaggaca	cggccaacgt	cacagtcaact	gtgctgtcca	240
ccaagcagac	agaagactac	tgcctcgcat	ccaacaangt	gggtcgctgc	cggggctctt	300
tcccacgctg	gtactatgac	cccacggagc	agatctgcaa	gagtttctgt	tatggaggct	360


```

gcttgggcaa caagaacaac taccttcggg aagaagagtg cattctancc tgtcnggggtg      420
tgcaaggtgg gcctttgana ngcanctctg gggctcangc gactttcccc cagggccctt      480
ccatggaaaag ggcgccatcca ntgttctctg gcacctgtca gcccacccag ttccgctgca      540
ncaatggctg ctgcatcnac antttcctng aattgtgaca acacccccca ntgcccccaa      600
ccctcccaac aaagcttccc tgttnaaaaa tacnccantt ggcttttnac aaacncccg      660
cncctcctt ttccccnntn aacaaagggc nctngccttt gaactgceen aaccnnggaa      720
tctnccnngg aaaaantncc ccccttggtt cctnnaance cctccncaa anctncccc      780
ccc

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<210> 16
<211> 801
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(801)
<223> n = A,T,C or G

```

```

<400> 16
gccccaatc cagctgccac accaccacg gtgactgcat tagttcggat gtcatacaaa      60
agctgattga agcaaccctc tacttttttg togtgagcct tttgcttggt gcaggtttca      120
ttggctgtgt tggtagctgt gtcattgcaa cagaatgggg gaaaggcact gttctctttg      180
aagtaggggtg agtcctcaaa atccgtatag ttgggtgaagc cacagcactt gagccctttc      240
atgggtgtgt tccacacttg agtgaagtct tcttggaac cataatcttt cttgatggca      300
ggcactacca gcaacgtcag gaagtgtca gccattgttg tgtacaccaa ggcgaccaca      360
gcagctgcaa cctcagcaat gaagatgagg aggaggatga agaagaacgt cncgagggca      420
cacttgcctc ccgtcttagc accatagcag cccangaaac caagagcaaa gaccacaacg      480
ccngctgcga atgaaagaaa ntaccacgt tgacaaaactg catggccact ggacgcagct      540
tggcccgaa atcttcagaa aagggtgccc ccatcgattg aacacccana tgccactgc      600
cnacagggct gcncncncn gaaagaatga gccattgaag aaggatcctc ntgggtcttaa      660
tgaactgaaa cctgcatgg tggccctgt tcagggtctc tggcagtga ttctganaaa      720
aaggaaacngc nttagcccc ccaaangana aaacaccccc ggggtgttgcc ctgaattggc      780
ggccaaggan ccctgccccn g

```

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<210> 17
<211> 740
<212> DNA
<213> Homo sapien

```

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<220>
<221> misc_feature
<222> (1)...(740)
<223> n = A,T,C or G

```

```

<400> 17
gtgagagcca ggcgtccctc tgcctgcca ctgagtggca acaccggga gctgttttgt      60
cctttgtgga gcctcagcag ttccctcttt cagaactcac tgccaagagc cctgaacagg      120
agccaccatg cagtgttca gcttcattaa gaccatgatg atcctcttca atttgcctat      180
ctttctgtgt ggtgcagccc tgttgccagt gggcatctgg gtgtcaatcg atggggcatc      240
ctttctgaag atcttcgggc cactgtcgtc cagtgccatg cagtttgtca acgtgggcta      300
cttcctcatc gcagccggcg ttgtggtctt tgccttggt ttccctgggt gctatggtgc      360
taagacggag agcaagtgtg cctcgtgac gttctcttcc atcctcctcc tcatcttcat      420
tgctgaagtt gcagctgctg tggtcgcctt ggtgtacacc acaatggctg aaccattcct      480
gacgttgctg gtantgctg ccatcaanaa agattatggg ttcccaggaa aaattcactc      540
aantntggaa caccnccatg aaaagggtc caatttctgn tggcttcccc aactataccg      600
gaattttgaa agantcnccc tacttccaaa aaaaaanant tgcctttnc ccenttctgt      660
tgcaatgaaa acntccaan acngccaatn aaaacctgcc cnnncaaaa ggntcncaaa      720

```

caaaaaaant nnaagggttn

740

<210> 18

<211> 802

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(802)

<223> n = A,T,C or G

<400> 18

ccgctgggtg	cgctgggtcca	gngnagccac	gaagcacgtc	agcatacaca	gcctcaatca	60
caagggtcttc	cagctgccgc	acattacgca	gggcaagagc	ctccagcaac	actgcatatg	120
ggatacactt	tacttttagca	gccagggtga	caactgagag	gtgtcgaagc	ttattcttct	180
gagcctctgt	tagtggagga	agattccggg	cttcagctaa	gtagtcagcg	tatgtcccat	240
aagcaaacac	tgtgagcagc	cggaaggtag	aggcaaagtc	actctcagcc	agctctctaa	300
cattgggcat	gtccagcagt	tctccaaaca	cgtagacacc	agnggcctcc	agcacctgat	360
ggatgagtgt	ggccagcgct	gcccccttgg	ccgacttggc	taggagcaga	aattgctcct	420
ggttctgccc	tgtcaccttc	acttccgcac	tcatactgct	actgagtgtg	ggggacttgg	480
gctcaggatg	tccagagacg	tggttccgcc	ccctcnctta	atgacaccgn	ccanncaacc	540
gtcggtctcc	gccgantgng	ttcgtcgtnc	ctgggtcagg	gtctgctggc	cnctacttgc	600
aancttcgtc	nggcccattg	aattcaccnc	accggaactn	gtangatcca	ctnnttctat	660
aaccggnccg	caccgcnntt	ggaactccac	tcttnttnc	tttacttgag	ggttaaggtc	720
acccttnccg	ttaccttggt	ccaaaccntn	ccntgtgtcg	anatngtnaa	tcnggncna	780
tnccancnc	atangaagcc	ng				802

<210> 19

<211> 731

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(731)

<223> n = A,T,C or G

<400> 19

cnaagcttcc	aggtnacggg	ccgnaancc	tgacccnagg	tancanaang	cagnncgcgg	60
gagcccaccg	tcacngggng	ngtctttat	nggagggggc	ggagccacat	cnctggacnt	120
cntgacccca	actccccncc	ncncantgca	gtgatgagtg	cagaactgaa	ggtnacgtgg	180
caggaaccaa	gancaaannc	tgctccnntc	caagtcggcn	nagggggcgg	ggctggccac	240
gcncatecnt	cnagtgtctgn	aaagccccnn	cctgtctact	tgtttgaga	acngcnnga	300
catgcccagn	gttanataac	nggngagag	tnantttgcc	tctcccttcc	ggctgcgcgn	360
cngtntgtct	tagnggacat	aacctgacta	cttaactgaa	cccnngaata	tnccnccct	420
ccactaagct	cagaacaaaa	aacttcgaca	ccactcantt	gtcacctgnc	tgctcaagta	480
aagtgtaccc	catncccaat	gtntgctnga	ngetctgncc	tgcnttangt	tcggctcctgg	540
gaagacctat	caattnaagc	tatgtttctg	actgcctctt	gtccctgna	acaanccacc	600
cnncnntcca	agggggggnc	ggcccccaat	ccccccaacc	ntnaattnan	tttancccn	660
ccccnggcc	cggtcttcta	cnancntcnn	nnaacnggna	aaaccnnngc	tttncccaac	720
nnaatcnc	t					731

<210> 20

<211> 754

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(754)
 <223> n = A,T,C or G

<400> 20
 ,tttttttttt tttttttttt taaaaacccc ctccattnaa tgnaaacttc cgaaattgtc 60
 caacccccctc ntccaaatnn ccntttccgg gnggggggttc caaacccaan ttannttttg 120
 annttaaatt aaatnttntt tggnggnnna anccnaatgt nangaaagtt naaccanta 180
 tnancctnaa tncctggaaa ccngtngntt ccaaaaatnt ttaaccctta antccctccg 240
 aaatngttna nggaaaaccc aanttctcnt aagggtgttt gaaggntnaa tnaaaanccc 300
 nnccaattgt ttttngccac gcctgaatta attggnttcc gntgttttcc nttaaaanaa 360
 ggnaancccc ggttantnaa tccccccnnc cccaattata ccganttttt ttngaattgg 420
 gancccnccg gaattaacgg ggnnnttccc tnttgggggg cnggnncccc cccntccggg 480
 ggttnggggc aggnccnaat tgtttaaggg tccgaaaaat cctccnaga aaaaaanctc 540
 ccaggntgag nntnggggtt ncccccccc canggccctt ctcgnanagt tgggggtttg 600
 ggggcctggg attttnttcc cccnttntcc tcccccccc ccnggganag aggttngngt 660
 tttgntcnnc ggccccnccn aaganctttn ccganttnan ttaaatecnt gcctnggcga 720
 agtcnttgn agggntaaan ggccccctnn cggg 754

<210> 21
 <211> 755
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(755)
 <223> n = A,T,C or G

<400> 21
 atcancccat gacccnaac nngggaccnc tcanceggnc nnnnacnccn cggecnatca 60
 nngtnagnnc actncnnttn natcacnccc cnccnactac gccnncnanc cnacgcnceta 120
 nncanatncc actganngcg cganngtnan ngagaaanct nataccanag ncaccanacn 180
 ccagctgtcc nanaangcct nnnatacnng nnnatccaat ntgnancctc cnaagtattn 240
 nncnnanact gattttcctn anccgattac ccntncccc tanccctcc cccccaacna 300
 cgaaggcnct ggncnnaagg nngcncnccc ccgctagntc cccnncnaagt cncncncta 360
 aactcancn nattaacncc ttcttgagta tcaactcccg aatctcacc tactcaactc 420
 aaaaanactn gatacaaaat aatncaagcc tgnttatnac actntgactg ggtctctatt 480
 ttagnngtcc ntnaancntc ctaatacttc cagctcncct tcnccaattt ccnaanggct 540
 ctttcngaca gcatnttttg gttcccnntt gggttcttan ngaattgcc ttctntgaac 600
 gggctentct tttccttcgg ttancctggg ttcnncggc cagttattat tccccnttt 660
 aaattcntnc cntttanttt tggcnttcna aacccccggc cttgaaaacg gccccctggt 720
 aaaaggttgt tttganaaaa tttttgtttt gttcc 755

<210> 22
 <211> 849
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(849)
 <223> n = A,T,C or G

<400> 22
 tttttttttt tttttangtg tngtcgtgca ggtagagget tactacaant gtgaanacgt 60
 acgctnggan taangcgacc cgantttctag ganncnccct aaaatcanac tgtgaagatn 120

atcctgnnna	cggaanggtc	accggnngat	nttgctaggg	tgncenctec	cannncnttn	180
cataacteng	nggccctgcc	caaccacctc	ggcggccng	ngncegggcc	cgggtcattn	240
gnnttaaccn	cactnngcna	ncgggttccn	nccccnncng	accnnggcga	tccggggtn	300
tctgtcttcc	cctgnagncn	anaaantggg	ccnccgnccc	ctttaccct	nnacaagcca	360
cngccntcta	ncnccngccc	cccctccant	nnnggggact	gccnanngct	ccgttntctng	420
nnaccccnnn	gggtncctcg	gttgctcgant	cnaccgnang	ccanggatc	cnaaggaagg	480
tgcgttnttg	gccccctacc	ttcgctnccg	nncacccttc	ccgacnanga	nccgctcccg	540
cnccnccngg	cctcncctcg	caacacccgc	netctcngt	ncggnncccc	ccccacccgc	600
nccctcncnc	ngnccgnanc	ctccnccncc	gtctcannca	ccaccccgcc	ccgccaggcc	660
ntcanccacn	ggnggacnng	nagcncntc	gcncgcgcg	gcgnccct	cgcncngaa	720
ctnctcngg	ccantnccgc	tcaanccna	cnaaacgcgc	ctgcgcggcc	cgnagcgncc	780
ncctcncga	gtcctcccg	cttcnacc	angnttccn	cgaggacacn	nnaccccgcc	840
nncangcgg						849

<210> 23

<211> 872

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(872)

<223> n = A,T,C or G

<400> 23

gcgcaacta	tacttcgctc	gnactcgctc	gcctcgctnc	tcttttctc	cgcaaccatg	60
tctgacnanc	ccgattnggc	ngatatacn	aagntcganc	agtccaaact	gantaacaca	120
cacacnanc	aganaaatcc	netgccttcc	anagtanacn	attgaacnng	agaaccangc	180
nggcgaatcg	taatnaggcg	tgcgccgcca	atntgtcncc	gtttattntn	ccagctcnc	240
ctnccnacc	tactcttcn	nagctgtcnn	acccctngtn	cgnaccccc	naggtcgcca	300
tccgggtttn	nntgaccgng	cnccccctcc	ccccctccat	nacganccnc	ccgcaccacc	360
nanngcncg	ccccggnct	cttcgcnc	ctgtcctntn	ccccgtngc	ctggcnngn	420
accgcattga	ccctcgccnn	ctncnngaaa	ncgnanacgt	ccgggttggn	annancgctg	480
tgggnnngcg	tctgcnccgc	gttccttcn	ncnncttoca	ccatcttct	tacngggctc	540
ccncccntc	ctnnncacnc	cctgggagcg	tntcctntgc	cccccttnac	tccccctt	600
cgnccgtgnc	cgccccacc	ntcatttnca	nacgntcttc	acaannncct	ggntnncctc	660
cnancngnnc	gtcancnag	ggaaggngg	ggnnccnntg	nttgacgttg	ngngangtc	720
cgaanantcc	tccccntcan	cctacccct	cgggcgnnct	ctcngttnc	aacttancaa	780
ntctcccccg	ngngcncntc	tcagcctcnc	ccccccnct	ctctgcantg	tnctctgctc	840
tnaccnntac	gantnttcgn	cncctcttt	cc			872

<210> 24

<211> 815

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(815)

<223> n = A,T,C or G

<400> 24

gcatgcaagc	ttgagtattc	tatagngtca	cctaaatanc	ttggcntaat	catggtcnta	60
nctgncttcc	tgtgtcaaat	gtatacnaa	tanatatgaa	tctnatntga	caaganngta	120
tcntncatta	gtaacaantg	tnntgtccat	cctgtcngan	canattccca	tnnattnccn	180
cgcattcncn	gcncantatn	taatngggaa	ntcnntnnn	ncaccnncat	ctatcctncc	240
gcncctgac	tggnagagat	ggatnanttc	tnntntgacc	nacatgttca	tcttggtatn	300
aanaccccc	cgcnccac	cggttngng	cnagccnntc	ccaagacctc	ctgtggaggt	360

```

aacctgcgtc aganncatca aacntgggaa acccgcnnc angtnnaagt ngnnncanan 420
gatcccgccc agnnttnacc atcccttcnc agcgccccct ttngtgcctt anagnnagc 480
gtgtccnanc cnetcaacat ganacgcgcc agnccanccg caattnggca caatgtcgnc 540
gaaccccccta gggggantna tncaaanccc caggattgtc cncncangaa atcccnanc 600
cccncctac ccncttttg gacngtgacc aantcccga gtnccagtc ggcngnctc 660
ccccaccggt nncntgggg ggtgaanct cngnntcanc cngncgaggn ntcgnaagga 720
accggncctn ggncgaanng ancntcnga agngcncnt cgtataaccc cccctcncca 780
nccnacngnt agntcccccc cngggtncgg aangg 815

```

```

<210> 25
<211> 775
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(775)
<223> n = A,T,C or G

```

```

<400> 25
ccgagatgtc tcgtccgtg gccttagctg tgctcgcgt actctctctt tctggcctgg 60
aggctatcca gcgtactcca aagattcagg tttactcacg tcatccagca gagaatggaa 120
agtcaaattt cctgaattgc tatgtgtctg ggtttcatcc atccgacatt gaanttgact 180
tactgaagaa tgganagaga attgaaaaag tggagcattc agacttgtct ttcagcaagg 240
actggtcttt ctatctcntg tactacactg aattcacccc cactgaaaaa gatgagtatg 300
cctgccgtgt gaaccatgtg actttgtcac agcccaagat agttaagtgg gatcgagaca 360
tgtaagcagn cncatggaa gtttgaagat gccgcattht gattggatga attccaaatt 420
ctgcttgctt gcnttttaat antgatatgc ntatacacc taccctttat gnceccaaat 480
tgtagggggt acatnantgt tcnctnnga catgatcttc ctttataant ccnccnttcg 540
aattgccgt cncncngtn ngaatgtttc cnaaaccacg gttggctccc ccaggtcncc 600
tcttacggaa gggcctgggc cnccttncaa ggttggggga accnaaaatt tcnctntgc 660
cncncncca cnntcttng nncncanttt ggaacccttc cnattccctt tggcctcna 720
nccttnncta anaaaacttn aaancgtngc naaannttn acttcccccc ttacc 775

```

```

<210> 26
<211> 820
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(820)
<223> n = A,T,C or G

```

```

<400> 26
anattantac agtgtaatct tttcccagag gtgtgtanag ggaacggggc ctagaggcat 60
cccanagata ncttatanca acagtgtctt gaccaagagc tgctgggcac atttcttgca 120
gaaaagggtg cgggtcccat cactcctcct ctcccatagc catcccagag gggtagtag 180
ccatcangcc ttcggtggga gggagtcang gaaacaacan accacagagc anacagacca 240
ntgatgacca tgggcgggag cgagcctctt ccctgnaccg gggtaggana nganagccta 300
nctgaggggt cacactataa acgttaacga ccnagatnan cactgtcttc aagtgcaccc 360
ttcctacctg acnaccagng accnnnaact gcngcctggg gacagcncgt ggancagcta 420
acnnagcact cacctgcccc cccatggccc tncgntccc tggctctgnc aagggagct 480
ccctgttgga attncgggga naccaaggga nccccctcct ccantgtga agggaaaann 540
gatggaattt tnccttccg gccnntccc tcttcttta caegccccct nntactctc 600
tccctctntt ntcctgncnc acttttnacc ccnnnatttc ccttnattga tcggannctn 660
ganattccac tnnegcctnc cntcnatcng naanacnaaa nactntctna cccnggggat 720
gggnncctcg ntcatectct ctttttcnct accnccnntt ctttgctct ccttngatca 780

```

tccaacntc gntggccntn ccccccnnn tcctttncce

820

<210> 27

<211> 818

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(818)

<223> n = A,T,C or G

<400> 27

tctgggtgat	ggcctcttcc	tcctcagga	cctctgactg	ctctgggcca	aagaatctct	60
tgtttcttct	ccgagcccca	ggcagcgggtg	attcagccct	gccaacctg	attctgatga	120
ctgctgagtc	tgtgacggac	ccaaggggca	aatagggtcc	caggggtccag	ggaggggcgc	180
ctgctgagca	cttccgcccc	tcacctgcc	cagccctgc	catgagctct	gggctgggtc	240
tccgctcca	gggttctgct	cttccangca	ngccancaa	tggcgtggg	ccacactggc	300
ttcttctgc	ccctccctg	gctctganc	tctgtcttcc	tgctctgtgc	angcnccttg	360
gatctcagtt	tcctcncctc	anngaactct	gtttctgann	tcttcantta	actntgantt	420
tatnaccnan	tggctgtnc	tgctcnactt	taatgggcn	gaccggctaa	tcctcctctc	480
netcccttcc	anttcnnna	accngcttnc	cntctctcc	ccntancccg	ccnggggaanc	540
ctcctttgcc	ctnaccangg	gccnnnaccg	ccctnnctn	ggggggcng	gtnnctncnc	600
ctgntnnccc	cncctcncnt	tncctcgtcc	cnnccnccn	nngcannttc	ncngtcccn	660
tnnctcttcn	ngntctgnaa	ngntcncntn	tnnnnnngcn	ngntnntn	tcctctcnc	720
cnnntgnang	tnnttnnnnc	ncngnncccc	nnnnnnnnn	nggnntnnn	tctnccngc	780
ccnncccc	ngnattaagg	cctcncctc	ccggccnc			818

<210> 28

<211> 731

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(731)

<223> n = A,T,C or G

<400> 28

aggaagggcg	gagggatatt	gtangggatt	gagggatagg	agnataangg	gggaggtgtg	60
tcccaacatg	anggtgnngt	tctcttttga	angaggggtg	ngtttttann	ccnggtgggt	120
gattnaaccc	cattgtatgg	agnnaaaggn	tttnagggat	tttctggctc	ttatcagtat	180
ntanattcct	gtnaatcgga	aaatnatntt	tcnncnggaa	aatnttgctc	ccatccgnaa	240
attncctccg	ggtagtgcac	nttngggggn	cngccangtt	tcccaggtcg	ctanaatcgt	300
actaaagntt	naagtgggan	tncaaatgaa	aacctnncac	agagnatccn	taccgactg	360
tnnnttncct	tcgcccctng	actctgcng	agcccaatac	ccnngngnat	gtcncncngn	420
nnngcgnenc	tgaaannnnc	tcgnggctnn	gancatcang	gggtttcgca	tcaaaagcnn	480
cgtttencat	naaggcactt	tngcctcatc	caaccnctng	ccctcnncca	tttngccgtc	540
nggttncct	acgctnntng	cncctnnntn	ganattttnc	ccgctnggg	naancctcct	600
gnaatgggta	gggnccttntc	tttnaccnn	gnggtntact	aatcnnctnc	acgentnctt	660
tctcnacccc	cccccttttt	caatcccanc	ggcnaatggg	gtctccccnn	cgangggggg	720
nnnccannnc	c					731

<210> 29

<211> 822

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (822)
 <223> n = A,T,C or G

<400> 29
 actagtccag tgtgggtggaa ttccattgtg ttgggggncnc ttctatgant antnttagat 60
 cgctcanacc tcacancctc ccnacnangc ctataangaa nannaataga nctgtncnnt 120
 atntntacnc tcatannect cnnnaccac tccctcttaa cccntactgt gcctatngcn 180
 tnnctantct ntggcgectn cnanccaccn gtggggccnac cncnngnatt ctcnatctcc 240
 tcnccatntn gcctananta ngtncatacc ctatacctac nccaatgcta nnnctaancn 300
 tccatnantt annntaacta ccaactgacnt ngactttcnc atnanctcct aatttgaatc 360
 tactctgact cccacngcct annnattagc ancntccccc nacnatntct caaccaaadc 420
 ntcaacaacc tatctantcg ttcnccaacc nttncctcgg atccccnnac aacccccctc 480
 ccaaataacc nccacctgac ncctaaccen caccatcccg gcaagccnan ggcatttan 540
 ccaactggaat cacnatngga naaaaaaac ccnaactctc tancncnnat ctccctaana 600
 aatnctectn naatttactn ncantnccat caancccaen tgaaacnnaa cccctgtttt 660
 tanatccctt ctttcgaaaa ccnacccttt annncccaac ctttngggcc cccccnctnc 720
 ccnaatgaag gncncccaat cnangaaacg nccntgaaaa ancnaggcna anannntccg 780
 canatcctat cccttanttn ggggncctt nccngggcc cc 822

<210> 30
 <211> 787
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (787)
 <223> n = A,T,C or G

<400> 30
 cggcgccctg ctctggcaca tgcctcctga atggcatcaa aagtgatgga ctgcccattg 60
 ctagagaaga cttctctccc tactgtcatt atggagccct gcagactgag ggctcccctt 120
 gtctgcagga tttgatgtct gaagtcgtgg agtgtggctt ggagctcctc atctacatna 180
 gctggaagcc ctggagggcc tctctcgcca gcctccccct tctctccacg ctctccangg 240
 acaccagggg ctcacggcag cccattatc ccagnangac atggtgtttc tccacgcgga 300
 cccatggggc ctgnaaggcc agggctcctt ttgacacat ctctcccgtc ctgcctggca 360
 ggccgtggga tccactantt ctanaacggn cgcaccncg gtgggagctc cagcttttgt 420
 tccnttaat gaaggttaat tgcncgcttg gcgtaatcat nggtcanaac tntttcctgt 480
 gtgaaattgt ttntccccct ncnattccnc ncnacatacn aaccgcggaan cataaagtgt 540
 taaagcctgg gggtngcctn nngaanaac tnaactcaat taattgcgtt ggctcatggc 600
 ccgctttccn ttcnggaaaa ctgtcntccc ctgcnttntt gaatcggccca cccccnggg 660
 aaaagcggtt tgcnttttng ggggntcctt ccncttcccc cctcnctaan cctnecgct 720
 cggtcgttnc nggtngcggg gaangggnat nnnctccnc naagggggng agnnngntat 780
 ccccaaa 822

<210> 31
 <211> 799
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (799)
 <223> n = A,T,C or G

<400> 31

```

tttttttttt tttttttggc gatgctactg ttttaattgca ggaggtgggg gtgtgtgtac      60
catgtaccag ggctattaga agcaagaagg aaggagggag ggcagagcgc cctgctgagc      120
aacaaaggac tcctgcagcc ttctctgtct gtctcttggc gcaggcacat ggggaggcct      180
cccgcagggg gggggccacc agtccagggg tgggagcact acanggggtg ggagtgggtg      240
gtggctggtn cnaatggcct gncacanatc cctacgattc ttgacacctg gatttcacca      300
ggggaccttc tgttctccca nggnaacttc ntnnatctcn aaagaacaca actgtttctt      360
cngcanttct ggctgttcat ggaaagcaca ggtgtccnat ttnggctggg acttggtaca      420
tatggttccg gccacctct cccntcnaaa aagtaattca ccccccccn ccntctnttg      480
cctgggccct taantacca caccggaact canttannta ttcactctng gntgggcttg      540
ntnatcnccn cctgaangcg ccaagttgaa aggccacgac gtncccnctc cccatagnan      600
nttttnnctn canctaatgc cccccnnggc aacnatccaa tcccccccn tgggggcccc      660
agcccgangc ccccgncctc ggnnnccngn cncgnantcc ccaggntctc ccantcngnc      720
ccnnngcncc cccgcacgca gaacanaagg ntngagccnc cgcannnnnn nggtnnncac      780
ctcgcccccc ccnnccngn

```

<210> 32

<211> 789

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(789)

<223> n = A,T,C or G

<400> 32

```

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt      60
tttttccnag ggcaggttta ttgacaacct cncgggacac aancaggctg gggacaggac      120
ggcaacaggc tccggcggcg gcggcggcgg ccttacctgc ggtaccaaata ntgcagcctc      180
cgctcccgtt tgatnttccct ctgcagctgc aggatgcctt aaaacagggc ctggccctn      240
ggtgggcacc ctgggatttn aatttccacg ggcacaatgc ggtcgcancc cctcaccacc      300
nattaggaat agtggtnnta cccnccnccg ttggcncact ccccntggaa accacttntc      360
gcggctcccg catctggtct taaaccttgc aaacnctggg gccctctttt tggttantnt      420
nccngccaca atcatnactc agactggcnc gggctggccc caaaaaancn ccccaaaacc      480
gncccatgtc tttnccgggt tgctgcnatn tncatcacct cccgggcnca ncaggncaac      540
ccaaaagttc ttgnggccn caaaaaanct ccggggggnc ccagtttcaa caaagtcac      600
ccccttggcc cccaaatcct ccccccgntt nctgggtttg ggaacccacg cctctnnctt      660
tggnnggcaa gntggntccc ccttcgggcc cccggtgggc ccnctcttaa ngaaaacncc      720
ntcctnnnca ccatcccccc nngnnacgnc tancaangna tccctttttt tanaaacggg      780
ccccccncc

```

<210> 33

<211> 793

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(793)

<223> n = A,T,C or G

<400> 33

```

gacagaacat gttggatggt ggagcacctt tctatacgac ttacaggaca gcagatgggg      60
aattcatggc tgttgagca atanaacccc agttctacga gctgtgata aaaggacttg      120
gactaaagtc tgatgaactt cccaatcaga tgagcatgga tgattggcca gaaatgaana      180
agaagtttgc agatgtattt gcaaagaaga cgaaggcaga gtggtgtcaa atctttgacg      240
gcacagatgc ctgtgtgact ccggttctga cttttgagga ggttggtcat catgatcaca      300
acaangaacg gggctcgttt atcaccantg aggagcagga cgtgagcccc cgccctgcac      360

```



```

ctctgctgtt aaacacccca gccatccctt ctttcaaaag ggatccacta cttctagagc 420
ggncgccacc gcggtggagc tccagctttt gttcccttta gtgagggtta attgcgcgct 480
tggcgtaatc atggtcatan ctgtttcctg tgtgaaattg ttatccgctc acaattccac 540
acaacatacg anccggaagc atnaaatttt aaagcctggn ggtngcctaa tgantgaact 600
nactcacatt aattggcttt gcgctcactg cccgcttttc agtccggaaa acctgtcctt 660
gccagctgcc nttaatgaat cnggccaccc cccggggaaa aggcngtttg cttnttgggg 720
cgcncttccc gctttctcgc ttcttgaant ccttcccccc ggtcttttcg cttgcggcna 780
acggtatcna cct 793

```

```

<210> 34
<211> 756
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(756)
<223> n = A,T,C or G

```

```

<400> 34
gccgcgaccg gcatgtacga gcaactcaag ggcgagtgga accgtaaaag cccaatctt 60
ancaagtgcg gggaanagct gggtcgactc aagctagttc ttctggagct caacttcttg 120
ccaaccacag ggaccaagct gaccaaacag cagctaattc tggcccgta catactggag 180
atcggggccc aatggagcat cctacgcaan gacatccctt ccttcgagcg ctacatggcc 240
cagctcaaat gctactactt tgattacaan gagcagctcc ccgagtcagc ctatatgcac 300
cagctcttgg gcctcaacct cctcttcctg ctgtcccaga accgggtggc tgantnccac 360
acgganttgg ancggtgcc tgcccanga catacanacc aatgtctaca tcnaccacca 420
gtgtcctgga gcaatactga tgganggcag ctaccncaa gtnttcctgg ccnagggtaa 480
catccccgcg cgagagctac accttcttca ttgacatcct gctcgacact atcagggatg 540
aaaatcgcn ggttgctcca gaaaggctnc aanaanatcc tttcnctga aggcccccg 600
atncnctagt nctagaatcg gcccgccatc gcggtgganc ctccaacctt tcgttnccct 660
ttactgaggg ttnattgccg cccttggcgt tatcatggtc acncnngtn cctgtgttga 720
aattnttaac cccccacaat tccacgcna cattng 756

```

```

<210> 35
<211> 834
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(834)
<223> n = A,T,C or G

```

```

<400> 35
ggggatctct anactnacct gnatgcatgg ttgtcggtgt ggtcgctgtc gatgaanatg 60
aacaggatct tgcccttgaa gctctcggtc gctgtnttta agttgctcag tctgccgtca 120
tagtcagaca cncctctggg caaaaaacan caggatntga gtcttgattt cacctccaat 180
aatcttcngg gctgtctgct cggtgaaact gatgacnang ggcagctggg tgtgtntgat 240
aaantccanc angttctect tggtagacct cccttcaaag ttgttccggc cttcatcaaa 300
ctcttnnaan angannanc canctttgtc gagctggnat ttgganaaca cgtcactgtt 360
ggaaactgat ccaaatggg atgtcatcca tcgcctctgc tgcctgcaaa aaacttgctt 420
ggcncaaact cgaactcccn tccttgaaag aagccnatca caccacctc cctggactcc 480
nncaangact ctnccgctnc ccntccnng cagggttggg ggcannccgg gccntgcgc 540
ttcttcagcc agttcacnat ntcatcagc ccctctgcca gctgtntat tccttggggg 600
gganccgctc tctcccttcc tgaannaact ttgaccgtng gaatagccgc gentcncnt 660
acntnctggg ccgggttcaa antccctccn ttgncnntcn cctcgggcca ttctggattt 720
nccnaacttt ttccttcccc cncctcncgg ngtttggntt tttcatnggg cccaactct 780

```

gctnttggcc antccccctgg gggcntntan cccccctnt ggtcccntng ggcc

834

<210> 36

<211> 814

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(814)

<223> n = A,T,C or G

<400> 36

cggnccgttt	cengccgcgc	cccgtttcca	tgacnaaggc	tcccttcang	ttaaatacnn	60
cctagnaaac	attaatgggt	tgctctacta	atacatcata	cnaaccagta	agcctgcccc	120
naacgccaac	tcaggccatt	cctaccaaag	gaagaaaggc	tggtctctcc	acccccgtga	180
ggaaaggcct	gccttgtaag	acaccacaat	ncggctgaat	ctnaagtctt	gtgttttact	240
aatggaaaaa	aaaaataaac	aanaggtttt	gttctcatgg	ctgcccaccg	cagcctggca	300
ctaaaacanc	ccagcgctca	cttctgcttg	ganaaatatt	ctttgctctt	ttggacatca	360
ggcttgatgg	tatcaactgcc	acntttccac	ccagctgggc	nccttccccc	catntttgtc	420
antgancctgg	aaggcctgaa	ncttagcttc	caaaagtctc	ngcccacaag	accggccacc	480
aggggangtc	ntttncagtg	gatctgccaa	anantaccn	tatcatcnnt	gaataaaaag	540
gccctgaac	ganatgcttc	cancancett	taagaccat	aatcctngaa	ccatggtgcc	600
cttcgggtct	gatecnaaag	gaatgttctt	gggtcccant	ccctccttg	ttncctacgt	660
tgntttggac	cctgtctngn	atnacccean	tganatcccc	ngaagcacc	tnccctggc	720
atttganttt	cntaaattct	ctgccctacn	nctgaaagca	cnattccctn	ggcncnnaa	780
ggngaactca	agaaggtctn	ngaaaaacca	cncn			814

<210> 37

<211> 760

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(760)

<223> n = A,T,C or G

<400> 37

gcattgctgt	cttcctcaaa	gttggtcttg	ttgccataac	aaccaccata	ggtaaagcgg	60
gcgcagtgtt	cgctgaagg	gttgtagtac	cagcgcgga	tgctctcctt	gcagagtcc	120
gtgtctggca	ggtccacgca	atgcccttg	tcaactggga	aatggatgcg	ctggagctcg	180
tcaanccac	tcgtgtattt	ttcacangca	gcctcctccg	aagctcccg	gcagtgggg	240
gtgtcgtcac	actccactaa	actgtcgatn	cancagccca	ttgctgcagc	ggaactgggt	300
gggctgacag	gtgccagaac	acactggatn	ggcctttcca	tggaagggcc	tgggggaaat	360
cncctnancc	caaaactgcct	ctcaaaggcc	accttgca	ccccgacagg	ctagaaatgc	420
actcttcttc	ccaaaggtag	ttgttcttg	tgcccaagca	ncctccanca	aaccaaanc	480
ttgcaaaatc	tgctccgtgg	gggtcatnnn	taccanggtt	ggggaaanaa	acccggcngn	540
gancncctt	gtttgaatgc	naaggnaata	atcctcctgt	cttgcttggg	tggaanagca	600
caattgaact	gttaacnttg	ggccngttc	cncnngggtg	gtctgaaact	aatcaccgtc	660
actggaaaaa	ggtagtgcc	ttccttgat	tcccgaant	cccctngntt	tggtgnntt	720
ctcctctncc	ctaaaaatcg	tnttcccccc	centanggcg			760

<210> 38

<211> 724

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(724)
 <223> n = A,T,C or G

<400> 38
 tttttttttt tttttttttt tttttttttt ttttttaaaa cccctccat tgaatgaaaa 60
 ctccnaaat tgtccaaccc cctcnccaa atnnccattt cggggggggg gttccaaacc 120
 caaattaatt ttgganttta aattaaatnt tnattnnggg aanaanccaa atgtnaagaa 180
 aatttaaccc attatnaact taaatnctn gaaaccctg gnttccaaaa atttttaacc 240
 cttaaattccc tccgaaattg ntaanggaaa accaaattcn cctaaggctn tttgaaagggt 300
 ngatttaaac ccccttnant tnttttnacc cnngnctnaa ntatttngnt tccggtgttt 360
 tccntttaan cntnggtaac tcccgnataat gaannnccct aanccaatta aaccgaattt 420
 tttttgaatt ggaaattccn ngggaattna cgggggtttt tccnttttg gggccatncc 480
 cccnctttcg ggggttggn ntaggttgaa tttttnnang ncccaaaaaa ncccccaana 540
 aaaaaactcc caagnnttaa ttngaantnc ccccttccca ggccttttg gaaagnggg 600
 tttntggggg ccngggantt cnttccccn ttncncccc cccccnggt aaanggttat 660
 ngnntttggt ttttgggccc cttnanggac ctccggatn gaaattaaat ccccggnccg 720
 gccg 724

<210> 39
 <211> 751
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(751)
 <223> n = A,T,C or G

<400> 39
 tttttttttt tttttctttg ctcacattta atttttattt tgattttttt taatgctgca 60
 caacacaata tttatttcat ttgtttcttt tatttcatth tatttgtttg ctgctgctgt 120
 tttatttatt tttactgaaa gtgagaggga acttttgtgg ccttttttcc tttttctgta 180
 ggccgcctta agcttttctaa atttggaaca tctaagcaag ctgaanggaa aaggggggtt 240
 cgcaaaatca ctggggggaa nggaaagggt gctttgttaa tcatgcccta tgggtgggtga 300
 ttaactgctt gtacaattac ntthcacttt taattaattg tgctnaangc ttaattana 360
 cttgggggtt ccttcccan accaaccnct ctgacaaaaa gtgcngccc tcaaatnatg 420
 tcccggcnnt cnttgaaaca cacngcngaa ngttctcatt ntccccncnc caggtnaaaa 480
 tgaagggtta ccatntttaa cncacctcc acntggcnnn gctgaatcc tcnaaaancn 540
 cctcaancn aattnctnng ccccggtcnc gcntnngtcc cnccegggt cggggaantn 600
 cacccccnga anncnntnnc naacnaaatt ccgaaaatat tccnntcnc tcaattcccc 660
 cnnagactnt cctcnncnan cncaattttc tttntntcac gaacncgnnc cnnaaatgn 720
 nnnncnctc cncnngtcn naatcnccan c 751

<210> 40
 <211> 753
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(753)
 <223> n = A,T,C or G

<400> 40
 gtggtatttt ctgtaagatc aggtgttcct ccctcgtagg ttttagaggaa acaccctcat 60
 agatgaaaac ccccccgaga cagcagcact gcaactgccca agcagccggg gtaggagggg 120

```

cgccctatgc acagctgggc ccttgagaca gcagggcttc gatgtcaggc tcgatgtcaa      180
tggctctggaa gcggcggtg tacctgcgta ggggcacacc gtcagggccc accaggaact      240
tctcaaagtt ccaggcaacn tcgttcgcac acaccggaga ccaggtgatn agcttgggggt      300
cggtcataaa cgggtggcg tcgtcgctgg gagctggcag gccctcccgc aggaaggcna      360
ataaaagggt gcggcccgca ccgttcantc cgcacttctc naanaccatg angttgggct      420
cnaaccacc accannccgg acttccttga nggaattccc aaatctcttc gntcttgggc      480
ttctnctgat gccctantc gttgcccn gn atgccaanca nccccancc cgggggtcct      540
aaancaccn cctctcntt tcactctgggt tntntcccc ggaccttggg tctctcaag      600
ggancccata tctcnaccan tactcaccnt nccccccnt gnnaccanc cttctanngn      660
tccccnccg ncctctggcc cntcaaan gcttnacna cctgggtctg ccttcccccc      720
tnccctatct gnacccnctn tttgtctcan tnt                                     753

```

<210> 41

<211> 341

<212> DNA

<213> Homo sapien

<400> 41

```

actatatcca tcacaacaga catgcttcat cccatagact tcttgacata gcttcaaagt      60
agtgaaccca tcttgattt atatacatat atgttctcag tattttggga gcctttccac      120
ttctttaaac cttgttcatt atgaacactg aaaataggaa tttgtgaaga gttaaaaagt      180
tatagcttgt ttacgtagta agtttttgaa gtctacattc aatccagaca cttagttgag      240
tgttaaactg tgatttttaa aaaatatcat ttgagaatat tctttcagag gtattttcat      300
ttttactttt tgattaattg tgttttatat attagggtag t                                     341

```

<210> 42

<211> 101

<212> DNA

<213> Homo sapien

<400> 42

```

acttactgaa tttagtctg tgctcttctt tatttagtgt tgtatcataa atactttgat      60
gtttcaaaca tcttaataa ataattttca gtggcttcat a                                     101

```

<210> 43

<211> 305

<212> DNA

<213> Homo sapien

<400> 43

```

acatctttgt tacagtctaa gatgtgttct taaatcacca ttccttctctg gtcctcaccc      60
tccaggggtg tctcacactg taattagagc tattgaggag tctttacagc aaattaagat      120
tcagatgcct tgctaagtct agagttctag agttatgttt cagaaagtct aagaaacca      180
cctcttgaga ggtcagtaaa gaggacttaa ttttcatat ctacaaaatg accacaggat      240
tggtacaga acgagagtta tcttgataa ctcagagctg agtacctgcc cgggggccgc      300
tcgaa                                     305

```

<210> 44

<211> 852

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (852)

<223> n = A,T,C or G

<400> 44

```

acataaatat cagagaaaag tagtctttga aatattttacg tccaggaggt ctttgtttct 60
gattatttgg tgtgtgtttt ggtttgtgtc caaagtattg gcagcttcag ttttcatttt 120
ctctccatcc tcgggcattc ttcccaaatt tatataccag tcttcgtcca tccacacgct 180
ccagaatttc tctttttag tagtatctca tagctcggt gagcttttca taggtcatgc 240
tgctgttgtt cttcttttta ccccatagct gagccactgc ctctgatttc aagaacctga 300
agacgccctc agatcgggtc tccatttta ttaactcctg gttcttgtct gggttcaaga 360
ggatgtcgcg gatgaattcc cataagtga tccctctcgg gttgtgcttt ttggtgtggc 420
acttggcagg ggggtcttgc tcttttttca tatcagggtga ctctgcaaca ggaagggtgac 480
tggtggttgt catggagatc tgagcccggc agaaagtttt gctgtccaac aaatctactg 540
tgctaccata gttggtgtca tataaatagt tctngtcttt ccagggtgtc atgatggaag 600
gctcagtttg ttcagtcttg acaatgacat tgtgtgtgga ctggaacagg tctactactgc 660
actggccgtt ccacttcaga tgctgcaagt tgctgtagag gagntgcccc gccgtccctg 720
ccgcccgggt gaactcctgc aaactcatgc tgcaaagggt ctgcgcgttg atgtcgaact 780
cntggaaaag gatacaattg gcatccagct ggttgggtgc caggaggtga tggagccact 840
cccacacctg gt 852

```

```

<210> 45
<211> 234
<212> DNA
<213> Homo sapien

```

```

<400> 45
acaacagacc cttgctcgtc aacgacctca tgctcatcaa gttggacgaa tccgtgtccg 60
agtctgacac catccggagc atcagcattg cttcgcagt ccctaccgcg gggaactctt 120
gcctcgtttc tggctggggt ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg 180
tgaacgtgtc ggtggtgtct gaggaggtct gcagtaagct ctatgaccgc ctgt 234

```

```

<210> 46
<211> 590
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(590)
<223> n = A,T,C or G

```

```

<400> 46
actttttatt taaatgttta taaggcagat ctatgagaat gatagaaaac atggtgtgta 60
atttgatagc aatattttgg agattacaga gttttagtaa ttaccaatta cacagttaaa 120
aagaagataa tatattccaa gcanatacaa aatatctaat gaaagatcaa ggcaggaaaa 180
tgantataac taattgacaa tggaaaatca attttaatgt gaattgcaca ttatccttta 240
aaagctttca aaanaaanaa ttattgcagt ctanttaatt caaacagtgt taaatggtat 300
caggataaan aactgaaggg canaaaagaat taattttcac ttcattgtaac ncaccanatt 360
ttacaatggc ttaaatgcan ggaaaaagca gtggaagtag ggaagtantc aaggctcttc 420
tggtctctaa tctgccttac tctttgggtg tggctttgat cctctggaga cagctgccag 480
ggctcctgtt atatccacaa tcccagcagc aagatgaagg gatgaaaaag gacacatgct 540
gccttccttt gaggagactt catctcactg gccaacactc agtcacatgt 590

```

```

<210> 47
<211> 774
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(774)
<223> n = A,T,C or G

```

```

<400> 47
acaagggggc ataatgaagg agtggggana gatttttaaag aaggaaaaaa aacgaggccc      60
tgaacagaat tttcctgnac aacggggcctt caaaataatt ttcttgggga ggttcaagac      120
gcttcaactgc ttgaaactta aatggatgtg ggacanaatt ttctgtaatg accctgaggg      180
cattacagac gggactcttg gaggaaggat aaacagaaag gggacaaagg ctaatcccaa      240
aacatcaaag aaaggaaggt ggcgtcatac ctcccagcct acacagtctt ccagggtctt      300
cctcatccct ggaggacgac agtggaggaa caactgacca tgtccccagg ctctgtgtgt      360
ctggctcctg gtcttcagcc cccagctctg gaagcccacc ctctgtgatg cctgctgtgg      420
ccacactcct tgaacacaca tcccagggtt atattcctgg acatggctga acctcctatt      480
cctacttccg agatgccttg ctccctgcag cctgtcaaaa tcccactcac cctccaaacc      540
acggcatggg aagcctttct gacttgcttg attactccag catcttggaa caatccctga      600
ttccccactc cttagaggca agataggggt gtttaagagta gggctggacc acttgagacc      660
aggctgctgg cttcaaattn tggctcattt acgagctatg ggaccttggg caagtnatct      720
tcacttctat gggcntcatt ttgttctacc tgcaaaatgg gggataataa tagt          774

<210> 48
<211> 124
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(124)
<223> n = A,T,C or G

<400> 48
canaaattga aattttataa aaaggcattt ttctettata tccataaaat gatataattt      60
ttgcaantat anaaatgtgt cataaattat aatgttctt aattacagct caacgcaact      120
tggt                                          124

<210> 49
<211> 147
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(147)
<223> n = A,T,C or G

<400> 49
gccgatgcta ctattttatt gcaggagggt ggggtgtttt tattattctc tcaacagctt      60
tgtggctaca ggtgggtgtct gactgcatna aaaanttttt tacgggtgat tgcaaaaatt      120
ttagggcacc catatcccaa gcantgt                                          147

<210> 50
<211> 107
<212> DNA
<213> Homo sapien

<400> 50
acattaaatt aataaaaagga ctgttggggg tctgctaaaa cacatggctt gatatatgtc      60
atggtttgag gttaggagga gttaggcata tgttttggga gaggggt          107

<210> 51
<211> 204
<212> DNA

```

<213> Homo sapien

<400> 51

```
gtcctaggaa gtctagggga cacacgactc tgggggtcacg gggccgacac acttgacagg      60
cggaaggaa aggcagagaa gtgacaccgt cagggggaaa tgacagaaag gaaaatcaag      120
gccttgcaag gtcagaaagg ggactcaggg ctccaccac agccctgccc cacttgacca      180
cctccctttt gggaccagca atgt                                           204
```

<210> 52

<211> 491

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(491)

<223> n = A,T,C or G

<400> 52

```
acaaagataa catttatctt ataacaaaaa tttgatagtt ttaaaggtta gtattgtgta      60
gggtattttc caaaagacta aagagataac tcaggtaaaa agttagaaat gtataaaaca      120
ccatcagaca ggttttttaa aaacaacata ttacaaaatt agacaatcat ctttaaaaaa      180
aaaacttctt gtatcaattt cttttgttca aaatgactga ctttaantatt tttaaatatt      240
tcanaaacac ttctcaaaa attttcaana tggtagcttt canatgtgcc ctcagtccca      300
atgttgctca gataaataaa tctcgtgaga acttaccacc caccacaagc tttctggggc      360
atgcaacagt gtcttttctt tcttttttct tttttttttt ttacaggcac agaaactcat      420
caattttatt tggataacaa aggggtctcca aatttatattg aaaaataaat ccaagttaat      480
atcactcttg t                                                         491
```

<210> 53

<211> 484

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(484)

<223> n = A,T,C or G

<400> 53

```
acataattta gcagggctaa ttaccataag atgctattta ttaanaggtn tatgatctga      60
gtattaacag ttgtgaagt ttggtatttt tatgcagcat tttctttttg ctttgataac      120
actacagaac ccttaaggac actgaaaatt agtaagtaa gttcagaaac attagctgct      180
caatcaaate tctacataac actatagtaa ttaaaacgtt aaaaaaaagt gttgaaatct      240
gcactagtat anaccgctcc tgtcaggata anactgcttt ggaacagaaa gggaaaaanc      300
agctttgant ttctttgtgc tgatangagg aaaggctgaa ttacctgtt gcctctccct      360
aatgattggc aggtcnggta aatnccaaaa catattccaa ctcaacactt cttttccncg      420
tancttgant ctgtgtattc caggancagg cggatggaat gggccagccc ncggatgttc      480
cant                                                                484
```

<210> 54

<211> 151

<212> DNA

<213> Homo sapien

<400> 54

```
actaaacctc gtgcttgta actccataca gaaaacgggtg ccatccctga acacggctgg      60
ccactgggta tactgtgac aaccgcaaca aaaaaaacac aaatccttgg cactggctag      120
```

tctatgtcct ctcaagtgcc tttttgtttg t 151

<210> 55
<211> 91
<212> DNA
<213> Homo sapien

<400> 55
acctggcttg tctccgggtg gttcccggcg cccccacgg tccccagaac_ggacactttc 60
gcctccagt ggatactcga gccaaagtgg t 91

<210> 56
<211> 133
<212> DNA
<213> Homo sapien

<400> 56
ggcggatgtg cggttggttat atacaaatat gtcattttat gtaagggact tgagtatact 60
tggatttttg gtatctgtgg gttgggggga cggtcagga accaatatcc catggatacc 120
aagggacaac tgt 133

<210> 57
<211> 147
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(147)
<223> n = A,T,C or G

<400> 57
actctggaga acctgagccg ctgctccgcc tctgggatga ggtgatgcan gcngtggcgc 60
gactgggagc tgagcccttc cctttgcgcc tgcctcagag gattgttgcc gacntgcana 120
tctcantggg ctggatncat gcagggt 147

<210> 58
<211> 198
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(198)
<223> n = A,T,C or G

<400> 58
acagggatat aggtttnaag ttattgtnat tgtaaaatac attgaatttt ctgtatactc 60
tgattacata catttactc ttaaaaaaga tgtaaatctt aatttttatg ccatctatta 120
attaccaat gagttacctt gtaaatgaga agtcatgata gcactgaatt ttaactagtt 180
ttgacttcta agtttggg 198

<210> 59
<211> 330
<212> DNA
<213> Homo sapien

<400> 59


```

acaacaaatg ggttgtgagg aagtcttata agcaaaactg gtgatggcta ctgaaaagat    60
ccattgaaaa ttatcattaa tgattttaaa tgacaagtta tcaaaaactc actcaatddd    120
cacctgtgct agcttgctaa aatgggagtt aactctagag caaatatagt atcttctgaa    180
tacagtcaat aaatgacaaa gccagggcct acaggtgggt tccagacttt ccagacccag    240
cagaaggaaat ctattttatc acatggatct ccgtctgtgc tcaaaatacc taatgatatt    300
tttcgtcttt attggacttc tttgaagagt                                330

```

```

<210> 60
<211> 175
<212> DNA
<213> Homo sapien

```

```

<400> 60
accgtgggtg ccttctacat tcttgacggc tcttcacca acatctgggt ctacttcggc    60
gtcgtgggct ccttctctct catctctatc cagctgggtc tgctcatcga ctttgcgcac    120
tcttggaacc agcgggtggct gggcaaggcc gaggagtgcg attcccggtc ctggt      175

```

```

<210> 61
<211> 154
<212> DNA
<213> Homo sapien

```

```

<400> 61
acccactttt tcttctgtg agcagtctgg acttctcact gctacatgat gagggtgagt    60
ggttggtgct cttcaacagt atctctccct ttcggatct gctgagccgg acagcagtgc    120
tggaactgcac agccccgggg ctccacattg ctgt                                154

```

```

<210> 62
<211> 30
<212> DNA
<213> Homo sapien

```

```

<400> 62
cgctcgagcc ctatagttag tcgtattaga                                30

```

```

<210> 63
<211> 89
<212> DNA
<213> Homo sapien

```

```

<400> 63
acaagtcatt tcagaccct ttgctcttca aaactgacca tcttttatat ttaatgcttc    60
ctgtatgaat aaaaatgggt atgtcaagt                                89

```

```

<210> 64
<211> 97
<212> DNA
<213> Homo sapien

```

```

<400> 64
accggagtaa ctgagtcggg acgctgaatc tgaatccacc aataaataaa ggttctgcag    60
aatcagtgca tccaggattg gtccttgat ctggggg                        97

```

```

<210> 65
<211> 377
<212> DNA
<213> Homo sapien

```

<220>
 <221> misc_feature
 <222> (1)...(377)
 <223> n = A,T,C or G

<400> 65
 acaacaanaa ntcccttctt taggccaactg atggaaacct ggaaccccct tttgatggca 60
 gcatggcgctc ctaggccttg acacagcggc tgggggtttg gctntcccaa accgcacacc 120
 ccaaccctgg tctaccacaca nttctggcta tgggctgtct ctgccactga acatcagggg 180
 tcggtcataa natgaaatcc caangggggac agaggtcagt agaggaaagt caatgagaaa 240
 ggtgctgttt gctcagccag aaaacagctg cctggcattc gccgctgaac tatgaacccg 300
 tgggggtgaa ctacccccan gaggaatcat gcctgggcga tgcaanggtg ccaacaggag 360
 gggcgggagg agcatgt 377

<210> 66
 <211> 305
 <212> DNA
 <213> Homo sapien

<400> 66
 acgcctttcc ctcagaattc agggaagaga ctgtgcctg ccttcctccg ttgttgctg 60
 agaacccgtg tgccccttcc caccatatcc accctcgctc catctttgaa ctcaaacacg 120
 aggaactaac tgcaccctgg tctctctccc agtccccagt tcaccctcca tccctcacct 180
 tcttccactc taagggatat caacactgcc cagcacaggg gccctgaatt tatgtggttt 240
 ttatatattt ttttaataaga tgcactttat gtcatttttt aataaagtct gaagaattac 300
 tggtt 305

<210> 67
 <211> 385
 <212> DNA
 <213> Homo sapien

<400> 67
 actacacaca ctccacttgc ccttgtgaga cactttgtcc cagcacttta ggaatgctga 60
 ggtcggacca gccacatctc atgtgcaaga ttgccagca gacatcaggt ctgagagttc 120
 cctttttaaa aaaggggact tgcttaaaaa agaagtctag ccacgattgt gtagagcagc 180
 tgtgtctgtc tggagattca cttttgagag agttctctc tgagacctga tcttttagagg 240
 ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgcttg 300
 cctctcccag ggccccagcc tggccacacc tgcttacagg gcactctcag atgcccatac 360
 catagtttct gtgctagtgg accgt 385

<210> 68
 <211> 73
 <212> DNA
 <213> Homo sapien

<400> 68
 acttaaccag atatattttt accccagatg gggatattct ttgtaaaaaa tgaaaataaa 60
 gtttttttaa tgg 73

<210> 69
 <211> 536
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(536)

<223> n = A,T,C or G

<400> 69

actagtccag	tgtggtggaa	ttccattgtg	ttggggggctc	tcaccctcct	ctcctgcagc	60
tccagctttg	tgctctgcct	ctgaggagac	catggcccag	catctgagta	ccctgctgct	120
cctgctggcc	accctagctg	tggccctggc	ctggagcccc	aaggaggagg	ataggataat	180
cccggtgggc	atctataacg	cagacctcaa	tgatgagtg	gtacagcgtg	cccttcactt	240
cgccatcagc	gagtataaca	aggccaccaa	agatgactac	tacagacgtc	cgctgcgggt	300
actaagagcc	aggcaacaga	ccgttggggg	ggtgaattac	ttcttcgacg	tagagggtgg	360
ccgaaccata	tgtaccaagt	cccagcccaa	cttggacacc	tgtgccttcc	atgaacagcc	420
agaactgcag	aagaaacagt	tgtgctcttt	cgagatctac	gaagttccct	ggggagaaca	480
gaangtcctt	gggtgaaatc	caggtgtcaa	gaaatcctan	ggatctgttg	ccaggc	536

<210> 70

<211> 477

<212> DNA

<213> Homo sapien

<400> 70

atgacccta	acaggggccc	tctcagccct	cctaatagacc	tccggcctag	ccatgtgatt	60
tcacttccac	tccataacgc	tcttcatact	aggcctacta	accaacacac	taaccatata	120
ccaatgatgg	cgcgatgtaa	cacgagaaa	cacataccaa	ggccaccaca	caccacctgt	180
ccaaaaaggc	cttcgatacg	ggataatcct	atttattacc	tcagaagtgt	ttttcttcgc	240
agggattttt	ctgagccttt	taccactcca	gcttagcccc	taccccccaa	ctaggagggc	300
actggccccc	aacaggcatc	accccgttaa	atcccctaga	agtcccactc	ctaaacacat	360
ccgtattact	cgcatcagga	gtatcaatca	cctgagctca	ccatagtcta	atagaaaaca	420
accgaaacca	aattattcaa	agcactgctt	attacaattt	tactgggtct	ctatttt	477

<210> 71

<211> 533

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(533)

<223> n = A,T,C or G

<400> 71

agagctatag	gtacagtgtg	atctcagctt	tgcaaacaca	ttttctacat	agatagtact	60
aggtattaat	agatatgtaa	agaaagaaat	cacaccatta	ataatggtaa	gatttggttta	120
tgtgatttta	gtggtatttt	tggcaccctt	atatatgttt	tccaaacttt	cagcagtgat	180
attatttcca	taacttaaaa	agtgagtttg	aaaaagaaaa	tctccagcaa	gcattctcatt	240
taaataaaag	tttgtcatct	ttaaaaatac	agcaatatgt	gactttttta	aaaagctgtc	300
aaatagggtg	gaccctacta	ataattatta	gaaatacatt	taaaaacatc	gagtacctca	360
agtcagtttg	ccttgaaaaa	tatcaaatat	aactcttaga	gaaatgtaca	taaaagaatg	420
cttcgtaatt	ttggagtang	aggttccctc	ctcaattttg	tattttttaa	aagtacatgg	480
taaaaaaaaa	aattcacaac	agtatataag	gctgtaaaat	gaagaattct	gcc	533

<210> 72

<211> 511

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(511)

<223> n = A,T,C or G

<400> 72

tattacggaa aaacacacca cataattcaa ctancaaaga anactgcttc agggcgtgta	60
aaatgaaagg cttccaggca gttatctgat taaagaacac taaaagaggg acaaggctaa	120
aagccgcagg atgtctacac tatancaggc gctatctggg ttggctggag gagctgtgga	180
aaacatggan agattggtgc tgganatcgc cgtggctatt cctcattgtt attacanagt	240
gaggttctct gtgtgcccac tggtttgaaa accgttctnc aataatgata gaatagtaca	300
cacatgagaa ctgaaatggc ccaaaccag aaagaaagcc caactagatc ctcagaanac	360
gcttctaggg acaataaccg atgaagaaaa gatggcctcc ttgtgcccc gtctgttatg	420
atttctctcc attgcagcna naaacccgtt cttctaagca aacncagggtg atgatggcna	480
aaatacaccc cctcttgaag naccnggagg a	511

<210> 73

<211> 499

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(499)

<223> n = A,T,C or G

<400> 73

cagtgccagc actggtgcca gtaccagtac caataacagt gccagtgccca gtgccagcac	60
cagtgggtggc ttcagtgtct gtgccagcct gaccgccact ctcacatttg ggctcttcgc	120
tggccttggt ggagctgggt ccagcaccag tggcagctct ggtgcctgtg gtttctccta	180
caagtgatgat tttagatatt gttaatectg ccagtccttc tcttcaagcc agggtgcatc	240
ctcagaaacc tactcaacac agcactctag gcagccacta tcaatcaatt gaagttgaca	300
ctctgcatta aatctatttg ccatttctga aaaaaaaaaa aaaaaaaggc cggccgctcg	360
antctagagg gcccgtttaa acccgctgat cagcctcgac tgtgccttct anttgccagc	420
catctgttgt ttgcccctcc cccgntgcct tccttgaccc tggaaaagtgc cactcccatc	480
gtcctttcct aantaaat	499

<210> 74

<211> 537

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(537)

<223> n = A,T,C or G

<400> 74

tttcatagga gaacacactg aggagatact tgaagaattt ggattcagcc gcgaagagat	60
ttatcagctt aactcagata aaatcattga aagtaataag gtaaaagcta gtctctaact	120
tccaggccca cggtcaagt gaatttgaat actgcattta cagtgtagag taacacataa	180
cattgtatgc atggaaacat ggaggaacag tattacagtg tcctaccact ctaatcaaga	240
aaagaattac agactctgat tctacagtga tgattgaatt ctaaaaatgg taatcattag	300
ggcttttgat ttataanact ttgggtactt atactaaatt atggtagtta tactgccttc	360
cagtttgctt gatataattg ttgatattaa gattccttgac ttatatattg aatgggttct	420
actgaaaaan gaatgatata ttcttgaaga catcgatata catttattta cactcttgat	480
tctacaatgt agaaaatgaa ggaaatgcc caaattgtat ggtgataaaa gtcccgt	537

<210> 75

<211> 467

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(467)
 <223> n = A,T,C or G

<400> 75
 caaanacaat tgttcaaaag atgcaaataa tacactactg ctgcagctca caaacacctc 60
 tgcataattac acgtacctcc tctgtctcct caagtagtgt ggtctatctt gccatcatca 120
 cctgctgtct gcttagaaga acggctttct gctgcaangg agagaaatca taacagacgg 180
 tggcacaagg aggccatctt ttctctcatcg gttattgtcc ctagaagcgt cttctgagga 240
 tctagttggg ctttctttct gggtttgggc catttcantt ctcatgtgtg tactattcta 300
 tcattattgt ataacgggtt tcaaaccngt gggcacncag agaacctcac tctgtaataa 360
 caatgaggaa tagccacggg gatctccagc accaaatctc tccatgttnt tccagagctc 420
 ctccagccaa cccaaatagc cgctgctatn gtgtagaaca tccctgn 467

<210> 76
 <211> 400
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(400)
 <223> n = A,T,C or G

<400> 76
 aagctgacag cattcgggcc gagatgtctc gctccgtggc cttagctgtg ctgcgcgtac 60
 tctctctttc tggcctggag gctatccagc gtactccaaa gattcagggt tactcacgtc 120
 atccagcaga gaatggaaa tcaaatttcc tgaattgcta tgtgtctggg ttcatccat 180
 ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaagt gagcattcag 240
 acttgtcttt cagcaaggac tggctcttct atctcttgta ctacactgaa ttcaccccca 300
 ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng 360
 tttagtgagg tccanacatg taagcagcan catgggaggt 400

<210> 77
 <211> 248
 <212> DNA
 <213> Homo sapien

<400> 77
 ctggagtgcc ttggtgtttc aagccctgc aggaagcaga atgcaccttc tgaggcacct 60
 ccagctgccc cggcggggga tgcgaggctc ggagcacctc tgcccggctg tgattgctgc 120
 caggcactgt tcatctcagc tttctgttcc ctttgtctcc ggcaagcgt tctgctgaaa 180
 gttcatatct ggagcctgat gtcttaacga ataaaggctc catgctccac ccgaaaaaaa 240
 aaaaaaaaaa 248

<210> 78
 <211> 201
 <212> DNA
 <213> Homo sapien

<400> 78
 actagtccag tgtggtggaa ttccattgtg ttgggcccac cacaatggct acctttaaca 60
 tcaccagac cccgcctgc ccgtgcccac cgctgctgct aacgacagta tgatgcttac 120
 tctgtactc ggaaactatt tttatgtaat taatgtatgc tttctgttt ataatgcct 180
 gatttaaaaa aaaaaaaaaa a 201

<210> 79
 <211> 552
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(552)
 <223> n = A,T,C or G

<400> 79
 tccttttgtt aggtttttga gacaacccta gacctaaact gtgtcacaga cttctgaatg 60
 tttaggcagt gctagtaatt tcctcgtaat gattctgtta ttactttcct attctttatt 120
 cctctttcct ctgaagatta atgaagttga aaattgaggt ggataaatac aaaaaggtag 180
 tgtgatagta taagtatcta agtgcagatg aaagtgtgtt atatatatcc attcaaaatt 240
 atgcaagtta gtaattactc aggtttaact aaattacttt aatatgctgt tgaacctact 300
 ctgttccttg gctagaaaaa attataaaca ggactttgtt agtttgggaa gccaaattga 360
 taatattcta tgttctaaaa gttgggctat acataaanta tnaagaaata tggaaatttta 420
 ttcccaggaa tatggggttc atttatgaat antaccggg anagaagttt tgantnaaac 480
 cngttttggt taatacgtta atatgtcctn aatnaacaag gcntgactta tttccaaaaa 540
 aaaaaaaaaa aa 552

<210> 80
 <211> 476
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(476)
 <223> n = A,T,C or G

<400> 80
 acagggattt gagatgctaa ggccccagag atcgtttgat ccaaccctct tattttcaga 60
 ggggaaaatg gggcctagaa gttacagagc atctagctgg tgcgctggca cccctggcct 120
 cacacagact cccgagtagc tgggactaca ggcacacagt cactgaagca ggccctgttt 180
 gcaattcacg ttgccacctc caacttaaac attcttcata tgtgatgtcc ttagtcacta 240
 aggttaaact ttcccaccca gaaaaggcaa cttagataaa atcttagagt actttcatac 300
 tcttctaagt cctcttcag cctcactttg agtcctcctt gggggttgat aggaantntc 360
 tcttggttt ctcaataaaa tctctatcca tctcatgttt aatttgggtac gcntaaaaat 420
 gctgaaaaaa ttaaaatggt ctggtttcnc tttaaaaaaa aaaaaaaaaa aaaaaa 476

<210> 81
 <211> 232
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(232)
 <223> n = A,T,C or G

<400> 81
 tttttttttg tatgcentcn ctgtggngtt attgttgctg ccaccctgga ggagccagct 60
 ttctttctgta tctttctttt ctgggggatc ttcttggtc tggccctcca tcccagcct 120
 ctcatcccca tcttgcaactt ttgctagggg tggaggcgct ttcttggtag cccctcagag 180
 actcagtcag cggaataaag tcctaggggt ggggggtgtg gcaagccggc ct 232

<210> 82
 <211> 383
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (383)
 <223> n = A,T,C or G

<400> 82
 aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc 60
 agtaccagta ccaataacat gccagtgcc gtgccagcac cagtgggtggc ttcagtgtg 120
 gtgccagcct gaccgccact ctcacatttg ggctcttcgc tggccttggg ggagctggtg 180
 ccagcaccag tggcagctct ggtgcctgtg gtttctccta caagtgagat tttagatatt 240
 gttaatcctg ccagtctttc tcttcaagcc aggggtgcac ctcagaaacc tactcaacac 300
 agcactctng gcagccacta tcaatcaatt gaagttgaca ctctgcatta aatctatttg 360
 ccatttcaaa aaaaaaaaaa aaa 383

<210> 83
 <211> 494
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (494)
 <223> n = A,T,C or G

<400> 83
 accgaattgg gaccgctggc ttataagcga tcatgtcctc cagtattacc tcaacgagca 60
 gggagatcga gtctatacgc tgaagaaatt tgacccgatg ggacaacaga cctgtctcagc 120
 ccatcctgct cggttctccc cagatgacaa atactctcga caccgaatca ccatcaagaa 180
 acgcttcaag gtgctcatga cccagcaacc gcgcctgtgc ctctgagggg ccttaaactg 240
 atgtcttttc tgccacctgt taccctctcg agactccgta accaaactct tcggactgtg 300
 agccctgatg cctttttgccc agccatactc tttggcntcc agtctctcgt ggcgattgat 360
 tatgcttgtg tgaggcaatc atggtggcat caccatnaa gggaacacat ttganttttt 420
 tttncatat tttaaattac naccagaata ntccagaata aatgaattga aaaactctta 480
 aaaaaaaaaa aaaa 494

<210> 84
 <211> 380
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (380)
 <223> n = A,T,C or G

<400> 84
 gctggtagcc tatggcgtgg ccacggangg gctcctgagg cacgggacag tgacttccca 60
 agtatcctgc gccgcgtctt ctaccgtccc tacctgcaga tcttcgggca gattccccag 120
 gaggacatgg acgtggccct catggagcac agcaactgct cgtcggagcc cggcttcttg 180
 gcacaccctc ctggggccca ggcgggcacc tgcgtctccc agtatgcaa ctggctggtg 240
 gtgctgtccc tcgtcatctt cctgctcgtg gccaacatcc tgctggtcac ttgctcattg 300
 ccatgttcag ttacacattc ggcaaagtac agggcaacag cnatctctac tgggaaggcc 360
 agcgttnccg cctcatccgg 380

<210> 85
 <211> 481
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(481)
 <223> n = A,T,C or G

<400> 85
 gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggccctctcgc ttcataccgc 60
 tnccatcgctc atactgtagg ttgcccacca cctcctgcat cttggggcgcg ctaatatcca 120
 ggaaactctc aatcaagtca ccgtcnatna aacctgtggc tggttctgtc ttccgctcgg 180
 tgtgaaagga tctccagaag gagtgcctga tcttccccac acttttgatg actttattga 240
 gtcgattctg catgtccagc aggaggttgt accagctctc tgacagtga gtcaccagcc 300
 ctatcatgcc nttgaacgtg ccgaagaaca ccgagccttg tgtggggggg gnagtctcac 360
 ccagattctg cattaccaga nagccgtggc aaaaganatt gacaactcgc ccaggngngaa 420
 aaagaacacc tcttggaagt gctngccgct cctcgtecnt tggtggnngc gcntnccctt 480
 t 481

<210> 86
 <211> 472
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(472)
 <223> n = A,T,C or G

<400> 86
 aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgctg agaattcatt 60
 acttggaataa gcaacttnaa gcctggacac tggattataa attcacaata tgcaaacatt 120
 taaacagtgt gtcaatctgc tcccttactt tgtcatcacc agtctgggaa taagggtatg 180
 ccctattcac acctgtttaa agggcgctaa gcatttttga ttcaacatct ttttttttga 240
 cacaagtcgc aaaaaagcaa aagtaaacag ttnttaattt gttagccaat tcactttctt 300
 catgggacag agccatttga tttaaaaagc aaattgcata atattgagct ttgggagctg 360
 atatntgagc ggaagantag cttttctact tcaccagaca caactccttt catattggga 420
 tgttnacnaa agttatgtct cttacagatg ggatgctttt gtggcaattc tg 472

<210> 87
 <211> 413
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(413)
 <223> n = A,T,C or G

<400> 87
 agaaaccagt atctctnaaa acaacctctc ataccttgatg gacctaatat tgtgtgcgtg 60
 tgtgtgtgcg cgcattattat atagacaggc acatcttttt tacttttgta aaagcttatg 120
 cctcttttgg atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct 180
 ttgtcttctg tgtaaatggg actagagaaa acacctatnt tatgagtcaa tctagttngt 240
 ttatttcgac atgaaggaaa tttccagatn acaactctna caaactctcc cttgactagg 300


```

ggggacaaaag aaaagcanaa ctgaacatna gaaacaattn cctgggtgaga aattncataa    360
acagaaattg ggtngtatat tgaaanannng catcattnaa acgtttttttt ttt          413

```

```

<210> 88
<211> 448
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(448)
<223> n = A,T,C or G

```

```

<400> 88
cgcagcgggt cctctctatc tagctccagc ctctcgctgt ccccaactccc cgcgtcccgc    60
gtcctagccn accatggccg ggcccctgcg cgccccgctg ctctgtctgg ccatcctggc    120
cgtggccctg gccgtgagcc ccgcggccgg ctccagtcctc ggcaagccgc cgcgcctggt    180
gggaggccca tggaccccg cgtggaagaag aagggtgtgcg gcgtgcaactg gactttgccg    240
tcggcnanta caacaaaccc gcaacnactt ttaccnagcn cgcgctgcag gttgtgccgc    300
cccaancaaa ttgttactng gggttaantaa ttcttggaag ttgaacctgg gccaaacnng    360
tttaccagaa ccnagccaat tngaacaatt nccccctcat aacagcccct tttaaaaagg    420
gaancantcc tgntcttttc caaatTTT          448

```

```

<210> 89
<211> 463
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(463)
<223> n = A,T,C or G

```

```

<400> 89
gaattttgtg cactggccac tgtgatggaa ccattgggcc aggatgcttt gagtttatca    60
gtagtgattc tgccaaagtt ggtgttgtaa catgagtatg taaaatgtca aaaaattagc    120
agaggctctag gtctgcatat cagcagacag tttgtccgtg tattttgtag ccttgaagtt    180
ctcagtgaca agttnnttct gatgcgaagt tctnattcca gtgttttagt cctttgcac    240
tttnatgttn agacttgccct ctntnaaatt gcttttgnt tctgcaggta ctatctgtgg    300
tttaacaaaa tagaannact tctctgcttn gaanatttga atatcttaca tctnaaaatn    360
aattctctcc ccatannaaa acccangccc ttggganaat ttgaaaaang gntccttcnn    420
aattcnnana anttcagntn tcatacaaca naacngganc ccc          463

```

```

<210> 90
<211> 400
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(400)
<223> n = A,T,C or G

```

```

<400> 90
agggattgaa ggtctnttnt actgtcggac tgttcancca ccaactctac aagttgctgt    60
cttccactca ctgtctgtaa gcntnttaac ccagactgta tcttcataaa tagaacaat    120
tcttcaccag tcacatcttc taggaccttt ttggattcag ttagtataag ctcttccact    180
tcctttgtta agacttcac    tggtaaagtc ttaagttttg tagaaaggaa ttaattgct    240

```

```

cggtctcttaa caatgtcctc tccttgaagt atttggtga acaaccacc tnaagtcctt    300
ttgtgcatcc attttaaata tacttaatag ggcattggtn cactaggtta aattctgcaa    360
gagtcactctg tctgcaaaag ttgcgttagt atatctgcc      400

```

<210> 91

<211> 480

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (480)

<223> n = A,T,C or G

<400> 91

```

gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact    60
ggcttaccctt acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac   120
atgcctcttt gactaccgtg tgccagtgtt ggtgattctc acacacctcc nnccgctctt   180
tgtggaaaaa ctggcacttg nctggaacta gcaagacatc acttaciaat tccccacga    240
gacacttgaa aggtgtaaca aagcgactct tgcatgtgtt ttgtccctc cggcaccagt   300
tgtcaatact aaccgcgtgg ttgcctcca tcacatttgt gatctgtagc tctggataca   360
tctcctgaca gtactgaaga acttcttctt ttgtttcaaa agcaactctt ggtgcctgtt   420
ngatcagggtt cccatttccc agtccgaatg ttcacatggc atatnttact tccccaaaa    480

```

<210> 92

<211> 477

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (477)

<223> n = A,T,C or G

<400> 92

```

atacagccca natcccacca cgaagatgcg cttgttgact gagaacctga tgcggtcact    60
gggtcccgctg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcctt   120
cccacgcagg cagcagcggg gccggtcaat gaactccact cgtggcttgg ggttgacggt   180
taantgcagg aagaggctga ccacctcgcg gtccaccagg atgcccgact gtgcgggacc   240
tgcagcgaaa ctctcgatg gtcatgagcg ggaagcgaat gangccagg gccttgccca   300
gaaccttcgg cctgttctct ggcgtcacct gcagctgtcg ccgctnacac tcggcctcgg   360
accagcggac aaacggcggt gaacagccgc acctcacgga tgcccantgt gtgcgctcc    420
aggaacggcn ccagcgtgtc caggtcaatg tcggtgaanc ctccgcgggt aatggcg      477

```

<210> 93

<211> 377

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (377)

<223> n = A,T,C or G

<400> 93

```

gaacggctgg accttgctc gcattgtgct gctggcagga ataccttggc aagcagctcc    60
agtcagagca gcccagacc gctgccgcc gaagctaagc ctgcctctgg ccttccctc    120
cgctcaatg cagaaccant agtgggagca ctgtgttag agttaagagt gaacactgt      180

```

```

tgattttact tgggaatttc ctctgttata tagcttttcc caatgctaata ttccaaacaa      240
caacaacaaa ataacatggt tgctgtttna gttgtataaa agtangtgat tctgtatnta      300
aagaaaatat tactgttaca tatactgctt gcaantttctg tatttattgg tntctctggaa      360
ataaatatat tattaata                                     377

```

```

<210> 94
<211> 495
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(495)
<223> n = A,T,C or G

```

```

<400> 94
ccctttgagg gggttagggc cagttcccag tgggaagaaac aggccaggag aantgcgtgc      60
cgagctgang cagatttccc acagtgaccc cagagccctg ggctatagtc tctgaccct      120
ccaaggaaag accaccttct ggggacatgg gctggagggc aggacctaga ggcaccaagg      180
gaaggcccca ttccggggct gttccccgag gaggaaggga aggggctctg tgtgcccccc      240
acgaggaana ggccctgant cctgggatca nacaccctt cacgtgtatc cccacacaaa      300
tgcaagctca ccaagggtccc ctctcagtc cttccctaca ccctgaacgg nactggccc      360
acaccacccc agancancca cccgccatgg ggaatgtnt caaggaatcg cngggcaacg      420
tggaactctng tcccnnaagg gggcagaatc tccaatagan gganngaacc cttgctnana      480
aaaaaaaaana aaaaaa                                     495

```

```

<210> 95
<211> 472
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(472)
<223> n = A,T,C or G

```

```

<400> 95
ggttacttggt ttctattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc      60
cctctggaag ccttgccgag agcggacttt gtaattgttg gagaataact gctgaatttt      120
tagctgtttt gagttgattc gcaccactgc accacaactc aatatgaaaa ctatttnact      180
tatttattat cttgtgaaaa gtatacaatg aaaattttgt tcatactgta tttatcaagt      240
atgatgaaaa gcaatagata tatattcttt tattatgttn aattatgatt gccattatta      300
atcggaacaaa tgtggagtg atgttctttt cacagtaata tatgcctttt gtaacttcac      360
ttggttattt tattgtaaat gaattacaaa attcttaatt taagaaaatg gtangttata      420
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<210> 96
<211> 476
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(476)
<223> n = A,T,C or G

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<400> 96
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attcttcaca gtagatgatg aaagagtcct ccagtgtctt gngcanaatg ttctagntat 240
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gcaggtaact ctccagaaaa acngacaggg caggcttgca tgaaaaagtn acatctgcgt 420
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<210> 97
<211> 479
<212> DNA
<213> Homo sapien

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<220>
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<222> (1)...(479)
<223> n = A,T,C or G

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<400> 97
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caatcgcaaa tcaaaactca caagtgtcga tctgtttag atttagtgta ataagactta 180
gattgtgctc ctteggatat gattgtttct canatcttgg gcaatnttcc ttagtcaaat 240
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gtgattatna aattaatcac aaatttcact tatacctgct atcagcagct agaaaaacat 360
ntnnttttta natcaaagta ttttgtgttt ggaantgttn aaatgaaatc tgaatgtggg 420
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```

<210> 98
<211> 461
<212> DNA
<213> Homo sapien

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<400> 98
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ttaagaaaaa ctaccacatg ttgtgtatcc tggtgccggc cgtttatgaa ctgaccaccc 420
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<210> 99
<211> 171
<212> DNA
<213> Homo sapien

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<400> 99
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cgtgagaaa agccttctct agcgatctga gaggcgtgcc ttgggggtac c 171

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<210> 100
<211> 269
<212> DNA
<213> Homo sapien

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<400> 100

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aaggctgagc	tgacgccgca	gaggtcgtgt	cacgtcccac	gaccttgacg	ccgtcgggga	180
cagccggaac	agagcccggg	gaagcgggag	gcctcgggga	gcccctcggg	aagggcggcc	240
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<210> 101

<211> 405

<212> DNA

<213> Homo sapien

<400> 101

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<210> 102

<211> 470

<212> DNA

<213> Homo sapien

<400> 102

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<210> 103

<211> 581

<212> DNA

<213> Homo sapien

<400> 103

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gcttctctag	cctcatttcc	tagctcttat	ctactattag	taagtggctt	ttttcctaaa	360
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ccatttttagt	cactaaacga	tatcaaagt	ccagaatgca	aaaggtttgt	gaacatttat	540
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<210> 104

<211> 578

<212> DNA

<213> Homo sapien

<400> 104

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aaaggaacat	tttagcctg	ggtataatta	gctaattcac	tttacaagca	tttattagaa	540
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<211> 538

<212> DNA

<213> Homo sapien

<400> 105

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<210> 106

<211> 473

<212> DNA

<213> Homo sapien

<400> 106

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<210> 107

<211> 1621

<212> DNA

<213> Homo sapien

<400> 107

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tggtgagaat	ccgtatgcc	cgctgaatct	cctggctgac	tttctgtgtg	gtggccttat	480
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<210> 108

<211> 382

<212> PRT

<213> Homo sapien

<400> 108

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Arg Val Asp Arg Pro Gly Ser Arg Tyr Asp Val Ser Arg Leu Gly Arg
35     40     45
Gly Lys Arg Ser Leu Val Leu Asp Leu Lys Gln Pro Arg Gly Ala Ala
50     55     60
Val Leu Arg Arg Leu Cys Lys Arg Ser Asp Val Leu Leu Glu Pro Phe
65     70     75     80
Arg Arg Gly Val Met Glu Lys Leu Gln Leu Gly Pro Glu Ile Leu Gln
85     90     95
Arg Glu Asn Pro Arg Leu Ile Tyr Ala Arg Leu Ser Gly Phe Gly Gln
100    105    110
Ser Gly Ser Phe Cys Arg Leu Ala Gly His Asp Ile Asn Tyr Leu Ala
115    120    125
Leu Ser Gly Val Leu Ser Lys Ile Gly Arg Ser Gly Glu Asn Pro Tyr
130    135    140
Ala Pro Leu Asn Leu Leu Ala Asp Phe Ala Gly Gly Gly Leu Met Cys
145    150    155    160
Ala Leu Gly Ile Ile Met Ala Leu Phe Asp Arg Thr Arg Thr Asp Lys
165    170    175
Gly Gln Val Ile Asp Ala Asn Met Val Glu Gly Thr Ala Tyr Leu Ser
180    185    190
Ser Phe Leu Trp Lys Thr Gln Lys Ser Ser Leu Trp Glu Ala Pro Arg
195    200    205
Gly Gln Asn Met Leu Asp Gly Gly Ala Pro Phe Tyr Thr Thr Tyr Arg
210    215    220
Thr Ala Asp Gly Glu Phe Met Ala Val Gly Ala Ile Glu Pro Gln Phe
225    230    235    240
Tyr Glu Leu Leu Ile Lys Gly Leu Gly Leu Lys Ser Asp Glu Leu Pro
245    250    255

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Asn Gln Met Ser Met Asp Asp Trp Pro Glu Met Lys Lys Lys Phe Ala
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 Asp Val Phe Ala Lys Lys Thr Lys Ala Glu Trp Cys Gln Ile Phe Asp
 275 280 285
 Gly Thr Asp Ala Cys Val Thr Pro Val Leu Thr Phe Glu Glu Val Val
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 325 330 335
 Ile Pro Ser Phe Lys Arg Asp Pro Phe Ile Gly Glu His Thr Glu Glu
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<210> 109
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 <212> DNA
 <213> Homo sapien

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 <211> 3410
 <212> DNA
 <213> Homo sapien

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gaggtcttat	ctctcagggg	gggttttaagt	gcggtttgca	ataatgtcgt	cttatttatt	3240
tagcgggggtg	aatattttat	actgtaagtg	agcaatcaga	gtataatgtt	tatggtgaca	3300
aaattaaagg	ctttcttata	tgtttaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	3360
aaaaaaaaara	aaaaaaaaaa	aaaaaaaaaa	aaaaaaataa	aaaaaaaaaa		3410

<210> 111

<211> 1289

<212> DNA

<213> Homo sapien

<400> 111

agccaggcgt	ccctctgcct	gcccactcag	tggcaacacc	cgggagctgt	tttgtccttt	60
gtggagcctc	agcagttccc	tctttcagaa	ctcactgcc	agagccctga	acaggagcca	120
ccatgcagtg	cttcagcttc	attaagacca	tgatgatcct	cttcaatttg	ctcatctttc	180
tgtgtggtgc	atgccctggtg	gcagtgggca	tctgggtgtc	aatcgatggg	gcataccttc	240
tgaagatctt	cgggccactg	tcgtccagt	ccatgcagtt	tgtcaacgtg	ggctacttcc	300
tcacgcagc	cggcggtgtg	gtctttgtc	ttgggttctc	gggctgctat	gggtgtaaga	360
ctgagagcaa	gtgtgccctc	gtgacgttct	tcttcactcct	cctcctcatc	ttcattgctg	420
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tgctggtagt	gcctgccatc	aagaaagatt	atggttccca	ggaagacttc	actcaagtgt	540
ggaacaccac	catgaaaggg	ctcaagtgtc	gtggcttcac	caactatacg	gattttgagg	600
actcacccta	cttcaaagag	aacagtgcct	ttccccatt	ctgttgcaat	gacaacgtca	660
ccaacacagc	caatgaaacc	tgcaccaagc	aaaagggtca	cgaccaaaaa	gtagagggtt	720
gcttcaatca	gcttttgtat	gacatccgaa	ctaattgcagt	caccgtgggt	gggtgtggcag	780
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tacaataagt	ccacttctgc	ctctgccact	actgctgcc	catgggaact	gtgaaggagc	900
accctggcaa	gcagcagtga	ttgggggagg	ggacaggatc	taacaatgtc	acttgggcca	960
gaatggacct	gccctttctg	ctccagactt	ggggctagat	agggaccact	ccttttagcg	1020
atgctgact	ttccttccat	tggtgggtgg	atgggtgggg	ggcattccag	agcctctaag	1080
gtagccagtt	ctgttgccca	ttccccagt	ctattaaacc	cttgatatgc	cccctaggcc	1140
tagtggtgat	cccagtgtc	tactggggga	tgagagaaag	gcattttata	gcctgggcat	1200
aagtgaatc	agcagagcct	ctgggtggat	gtgtagaagg	cacttcaaaa	tgcataaacc	1260
tgttacaatg	ttaaaaaaaa	aaaaaaaaa				1289

<210> 112

<211> 315

<212> PRT

<213> Homo sapien

<400> 112

Met	Val	Phe	Thr	Val	Arg	Leu	Leu	His	Ile	Phe	Thr	Val	Asn	Lys	Gln
1				5				10					15		
Leu	Gly	Pro	Lys	Ile	Val	Ile	Val	Ser	Lys	Met	Met	Lys	Asp	Val	Phe
			20					25					30		
Phe	Phe	Leu	Phe	Phe	Leu	Gly	Val	Trp	Leu	Val	Ala	Tyr	Gly	Val	Ala
			35				40					45			
Thr	Glu	Gly	Leu	Leu	Arg	Pro	Arg	Asp	Ser	Asp	Phe	Pro	Ser	Ile	Leu
			50				55				60				
Arg	Arg	Val	Phe	Tyr	Arg	Pro	Tyr	Leu	Gln	Ile	Phe	Gly	Gln	Ile	Pro
65					70				75					80	
Gln	Glu	Asp	Met	Asp	Val	Ala	Leu	Met	Glu	His	Ser	Asn	Cys	Ser	Ser
			85					90					95		
Glu	Pro	Gly	Phe	Trp	Ala	His	Pro	Pro	Gly	Ala	Gln	Ala	Gly	Thr	Cys
			100				105					110			
Val	Ser	Gln	Tyr	Ala	Asn	Trp	Leu	Val	Val	Leu	Leu	Leu	Val	Ile	Phe
			115				120					125			
Leu	Leu	Val	Ala	Asn	Ile	Leu	Leu	Val	Asn	Leu	Leu	Ile	Ala	Met	Phe
			130				135					140			
Ser	Tyr	Thr	Phe	Gly	Lys	Val	Gln	Gly	Asn	Ser	Asp	Leu	Tyr	Trp	Lys
145					150				155					160	
Ala	Gln	Arg	Tyr	Arg	Leu	Ile	Arg	Glu	Phe	His	Ser	Arg	Pro	Ala	Leu
			165				170					175			
Ala	Pro	Pro	Phe	Ile	Val	Ile	Ser	His	Leu	Arg	Leu	Leu	Leu	Arg	Gln
			180				185					190			
Leu	Cys	Arg	Arg	Pro	Arg	Ser	Pro	Gln	Pro	Ser	Ser	Pro	Ala	Leu	Glu

```

      195              200              205
His Phe Arg Val Tyr Leu Ser Lys Glu Ala Glu Arg Lys Leu Leu Thr
  210              215              220
Trp Glu Ser Val His Lys Glu Asn Phe Leu Leu Ala Arg Ala Arg Asp
  225              230              235              240
Lys Arg Glu Ser Asp Ser Glu Arg Leu Lys Arg Thr Ser Gln Lys Val
      245              250              255
Asp Leu Ala Leu Lys Gln Leu Gly His Ile Arg Glu Tyr Glu Gln Arg
      260              265              270
Leu Lys Val Leu Glu Arg Glu Val Gln Gln Cys Ser Arg Val Leu Gly
      275              280              285
Trp Val Ala Glu Ala Leu Ser Arg Ser Ala Leu Leu Pro Pro Gly Gly
  290              295              300
Pro Pro Pro Pro Asp Leu Pro Gly Ser Lys Asp
  305              310              315

```

```

<210> 113
<211> 553
<212> PRT
<213> Homo sapien

```

```

      <400> 113
Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala
  1              5              10              15
Gln Leu Leu Leu Val Asn Leu Leu Thr Phe Gly Leu Glu Val Cys Leu
      20              25              30
Ala Ala Gly Ile Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val
      35              40              45
Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly
      50              55              60
Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly
  65              70              75              80
Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile
      85              90              95
Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu
      100              105              110
Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly
      115              120              125
Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu
      130              135              140
Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala
  145              150              155              160
Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr
      165              170              175
Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu
      180              185              190
Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu
      195              200              205
Thr Cys Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly
      210              215              220
Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His
  225              230              235              240
Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu
      245              250              255
Leu Pro Arg Leu His Gln Leu Cys Cys Arg Met Pro Arg Thr Leu Arg
      260              265              270
Arg Leu Phe Val Ala Glu Leu Cys Ser Trp Met Ala Leu Met Thr Phe
      275              280              285

```

Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu Gly Leu Tyr Gln Gly Val
 290 295 300
 Pro Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly
 305 310 315 320
 Val Arg Met Gly Ser Leu Gly Leu Phe Leu Gln Cys Ala Ile Ser Leu
 325 330 335
 Val Phe Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg
 340 345 350
 Ala Val Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala
 355 360 365
 Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu
 370 375 380
 Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala
 385 390 395 400
 Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly
 405 410 415
 Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu
 420 425 430
 Pro Gly Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala
 435 440 445
 Gly Gly Ser Gly Leu Leu Pro Pro Pro Ala Leu Cys Gly Ala Ser
 450 455 460
 Ala Cys Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala
 465 470 475 480
 Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp
 485 490 495
 Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser
 500 505 510
 Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala
 515 520 525
 Gly Leu Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp
 530 535 540
 Lys Ser Asp Leu Ala Lys Tyr Ser Ala
 545 550

<210> 114

<211> 241

<212> PRT

<213> Homo sapien

<400> 114

Met Gln Cys Phe Ser Phe Ile Lys Thr Met Met Ile Leu Phe Asn Leu
 1 5 10 15
 Leu Ile Phe Leu Cys Gly Ala Ala Leu Leu Ala Val Gly Ile Trp Val
 20 25 30
 Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser
 35 40 45
 Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly
 50 55 60
 Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr
 65 70 75 80
 Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Ile Leu Leu Leu Ile
 85 90 95
 Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr
 100 105 110
 Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys
 115 120 125
 Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met

130	135	140
Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp		
145	150	155
Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn		160
	165	170
Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala		175
	180	185
His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile		190
	195	200
Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly		205
	210	215
Leu Glu Leu Ala Ala Met Ile Val Ser Met Tyr Leu Tyr Cys Asn Leu		220
	225	230
Gln		235
		240

<210> 115
 <211> 366
 <212> DNA
 <213> Homo sapien

<400> 115
 gctctttctc tccctctctc tgaatttaaat tctttcaact tgcaatttgc aaggattaca 60
 catttcactg tgatgtatat tgtgttgcaa aaaaaaaaaa gtgtctttgt ttaaaattac 120
 ttggtttctg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga 180
 actggtagaa aaacatctga agagctagtc tatcagcatc tgacagggtga attggatggg 240
 tctcagaacc atttcaccca gacagcctgt ttctatcctg tttataaaat tagtttgggt 300
 tctctacatg cataacaaac cctgctccaa tctgtccatc aaaagtctgt gacttgaagt 360
 ttagtc 366

<210> 116
 <211> 282
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(282)
 <223> n = A,T,C or G

<400> 116
 acaaagatga accatttcct atattatagc aaaattaaaa tctaccgta ttctaattatt 60
 gagaaatgag atnaaacaca atnttataaa gtctacttag agaagatcaa gtgacctcaa 120
 agactttact attttcatat tttaagacac atgatttatc ctatttttagt aacctgggtc 180
 atacgttaaa caaaggataa tgtgaacagc agagaggatt tgttggcaga aaatctatgt 240
 tcaatctnga actatctana tcacagacat ttctattcct tt 282

<210> 117
 <211> 305
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(305)
 <223> n = A,T,C or G

<400> 117

```

acacatgtcg cttcactgcc ttcttagatg cttctgggtca acatanagga acagggacca      60
tatttatect ccctcctgaa acaattgcaa aataaniaca aatatatgaa acaattgcaa      120
aataaggcaa aatatatgaa acaacagggtc tcgagatatt ggaaatcagt caatgaagga      180
tactgatccc tgatcactgt cctaattgcag gatgtgggaa acagatgagg tcacctctgt      240
gactgcecca gcttactgcc tgtagagagt ttctangctg cagttcagac agggagaaat      300
tgggt                                           305

```

<210> 118

<211> 71

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(71)

<223> n = A,T,C or G

<400> 118

```

accaaggtgt ntgaatctct gacgtgggga tctctgatcc ccgcacaatc tgagtggaaa      60
aantectggg t                                           71

```

<210> 119

<211> 212

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(212)

<223> n = A,T,C or G

<400> 119

```

actccggttg gtgtcagcag cacgtggcat tgaacatngc aatgtggagc ccaaaccaca      60
gaaaatgggg tgaaattggc caactttcta tnaacttatg ttggcaantt tgccaccaac      120
agtaagctgg cccttctaataaaaagaaaat tgaaagggtt ctcactaanc ggaattaant      180
aatggantca aganactccc aggctcagc gt                                           212

```

<210> 120

<211> 90

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(90)

<223> n = A,T,C or G

<400> 120

```

actcgttgca natcaggggc ccccagagt caccgttgca ggagtccttc tggctcttgcc      60
ctccgccggc gcagaacatg ctggggtggg                                           90

```

<210> 121

<211> 218

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(218)

<223> n = A,T,C or G

<400> 121

tgtancgtga anacgacaga naggggtgtc aaaaatggag aanccttgaa gtcattttga	60
gaataagatt tgctaaaaga ttgggggcta aaacatgggt attgggagac atttctgaag	120
atatncangt aaattangga atgaattcat gggtcttttg ggaattcctt tacgatngcc	180
agcatanact tcatgtgggg atancagcta cccttgta	218

<210> 122

<211> 171

<212> DNA

<213> Homo sapien

<400> 122

taggggtgta tgcaactgta aggacaaaaa ttgagactca actggcttaa ccaataaagg	60
catttgtag ctcatggaac aggaagtcgg atgggtgggc atcttcagtg ctgcatgagt	120
caccaccccg gcgggggtcat ctgtgccaca ggtccctgtt gacagtgcgg t	171

<210> 123

<211> 76

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(76)

<223> n = A,T,C or G

<400> 123

tgtagcgtga agacnacaga atgggtgtgtg ctgtgctatc caggaacaca tttattatca	60
ttatcaanta ttgtgt	76

<210> 124

<211> 131

<212> DNA

<213> Homo sapien

<400> 124

acctttcccc aaggccaatg tctgtgtgtc taactggccg gctgcaggac agctgcaatt	60
caatgtgctg ggtcatatgg aggggaggag actctaaaat agccaatttt attctcttgg	120
ttaagatttg t	131

<210> 125

<211> 432

<212> DNA

<213> Homo sapien

<400> 125

actttatcta ctggctatga aatagatggt ggaaaattgc gttaccaact ataccactgg	60
cttgaaaaag aggtgatagc tcttcagagg acttgtgact ttgtctcaga tgctgaagaa	120
ctacagtctg catttggcag aaatgaagat gaatttggat taaatgagga tgctgaagat	180
ttgcctcacc aaacaaaagt gaaacaactg agagaaaatt ttcaggaaaa aagacagtgg	240
ctcttgaagt atcagtcact ttgagaatg tttcttagtt actgcatact tcatggatcc	300
catgggtggg gtcttgcac tgtaagaatg gaattgattt tgcttttgca agaattctcag	360
caggaaacat cagaaccact attttctagc cctctgtcag agcaaaccctc agtgcctctc	420
ctctttgtctt gt	432

<210> 126
<211> 112
<212> DNA
<213> Homo sapien

<400> 126
acacaacttg aatagtaaaa tagaaactga gctgaaattt ctaattcact ttctaaccat 60
agtaagaatg atatttcccc ccagggatca ccaaataattt ataaaaattt gt 112

<210> 127
<211> 54
<212> DNA
<213> Homo sapien

<400> 127
accacgaaac cacaacaag atggaagcat caatccactt gccaagcaca gcag 54

<210> 128
<211> 323
<212> DNA
<213> Homo sapien

<400> 128
acctcattag taattgtttt gttgtttcat ttttttctaa tgtctccctt ctaccagctc 60
acctgagata acagaatgaa aatggaagga cagccagatt tctcctttgc tctctgtcga 120
ttctctctga agtctagggtt acccattttg gggacccatt ataggcaata aacacagttc 180
ccaaagcatt tggacagttt cttgttgtgt tttagaatgg ttttcctttt tcttagcctt 240
ttcctgcaaa aggctcactc agtcccttgc ttgctcagtg gactgggctc cccagggcct 300
aggctgcctt cttttccatg tcc 323

<210> 129
<211> 192
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (192)
<223> n = A,T,C or G

<400> 129
acatacatgt gtgtatattt ttaaataatca cttttgtatc actctgactt tttagcatac 60
tgaaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcatc 120
tagcacattc atctgtgata naaagatagg tgagtttcat ttccttcacg ttggccaatg 180
gataaacaaa gt 192

<210> 130
<211> 362
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (362)
<223> n = A,T,C or G

<400> 130
ccctttttta tggaatgagt agactgtatg tttgaanatt tanccacaac ctctttgaca 60


```

tataatgacg caacaaaaag gtgctgttta gtcctatggg tcagtttatg cccctgacaa    120
gtttccattg tgttttgccg atcttctggc taatcgtggg atcctccatg ttattagtaa    180
ttctgtattc ctttttggtt acgcctggta gatgtaacct gctangaggc taactttata    240
cttatttaaa agctcttatt ttgtgggtcat taaaatggca atttatgtgc agcactttat    300
tgcagcagga agcacgtgtg gggttggttg aaagctcttt gctaacttta aaaagtaatg    360
gg

```

<210> 131

<211> 332

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (332)

<223> n = A,T,C or G

<400> 131

```

ctttttgaaa gatcgtgtcc actcctgtgg acatcttggt ttaatggagt ttcccatgca    60
gtangactgg tatggttgca gctgtccaga taaaaacatt tgaagagctc caaaatgaga    120
gttctcccag gttcgccctg ctgctccaag tctcagcagc agcctctttt aggaggcatc    180
ttctgaacta gattaaggca gcttgtaaat ctgatgtgat ttgggtttatt atccaactaa    240
cttccatctg ttatcactgg agaaagccca gactcccan gacnggtacg gattgtgggc    300
atanaaggat tgggtgaagc tggcgttgtg gt

```

<210> 132

<211> 322

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (322)

<223> n = A,T,C or G

<400> 132

```

acttttgcca ttttgtatat ataaacaatc ttgggacatt ctctgaaaa ctagggtgtcc    60
agtggctaag agaactcgat ttcaagcaat tctgaaagga aaaccagcat gacacagaat    120
ctcaaattcc caaacagggg ctctgtggga aaaatgaggg aggacctttg tatctcgggt    180
tttagcaagt taaaatgaan atgacaggaa aggccttatt atcaacaaag agaagagttg    240
ggatgcttct aaaaaaaact ttggtagaga aaataggaat gctnaatcct aggggaagcct    300
gtaacaatct acaattggtc ca

```

<210> 133

<211> 278

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (278)

<223> n = A,T,C or G

<400> 133

```

acaagccttc acaagtttaa ctaaattggg attaatcttt ctgtanttat ctgcataatt    60
cttggttttc tttccatctg gtccttgggt tgacaatttg tggaaacaac tctattgcta    120
ctatttaaaa aaaaacacaa atctttccct ttaagctatg ttnaattcaa actattcctg    180
ctattcctgt ttgtcaaaag aaattatatt tttcaaaata tgtntatttg tttgatgggt    240

```

cccacgaaac actaataaaa accacagaga ccagcctg

278

<210> 134

<211> 121

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(121)

<223> n = A,T,C or G

<400> 134

gtttanaaaa	cttgttttagc	tccatagagg	aaagaatggt	aaactttgta	ttttaaaaca	60
tgattctctg	aggttaaact	tggttttcaa	atgttatatt	tacttgtatt	ttgcttttgg	120
t						121

<210> 135

<211> 350

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(350)

<223> n = A,T,C or G

<400> 135

acttanaacc	atgcctagca	catcagaatc	cctcaaagaa	catcagtata	atcctataacc	60
atancaagt	gtgactggtt	aagcgtgcga	caaagggtcag	ctggcacatt	acttgtgtgc	120
aaacttgata	cttttgttct	aagtaggaac	tagtatacag	tncctaggan	tggtactcca	180
gggtgcccc	caactcctgc	agccgctcct	ctgtgccagn	ccctgnaagg	aaactttcgct	240
ccacctcaat	caagccctgg	gccatgctac	ctgcaattgg	ctgaacaaac	gtttgctgag	300
ttcccaagga	tgcaaagcct	ggtgctcaac	tcctggggcg	tcaactcagt		350

<210> 136

<211> 399

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(399)

<223> n = A,T,C or G

<400> 136

tgtaccgtga	agacgacaga	agttgcatgg	cagggacagg	gcagggccga	ggccagggtt	60
gctgtgattg	tatccgaata	ntcctcgtga	gaaaagataa	tgagatgacg	tgagcagcct	120
gcagacttgt	gtctgccttc	aanaagccag	acaggaaggc	cctgcctgdc	ttggctctga	180
cctggcgggc	agccagccag	ccacaggtgg	gcttcttctt	tttgtggtga	caacnccaag	240
aaaactgcag	aggcccagg	tcagggtgtna	gtgggtangt	gaccataaaa	caccaggtgc	300
tcccaggaac	ccgggcaaag	gccatcccc	cctacagcca	gcattgccac	tggcgtgatg	360
ggtgcagang	gatgaagcag	ccagntgttc	tgctgtggt			399

<210> 137

<211> 165

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(165)
 <223> n = A,T,C or G

<400> 137
 actggtgtgg tngggggtga tgctggtggt anaagttgan gtgacttcan gatggtgtgt 60
 ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga 120
 ttggctggtc ccactggtgg tcactgtcat tgggtggggt cctgt 165

<210> 138
 <211> 338
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(338)
 <223> n = A,T,C or G

<400> 138
 actcactgga atgccacatt cacaacagaa tcagaggtct gtgaaaacat taatggctcc 60
 ttaactttctc cagtaagaat cagggacttg aaatggaaac gttaacagcc acatgcccaa 120
 tgctgggcag tctcccatgc cttccacagt gaaagggctt gagaaaaatc acatccaatg 180
 tcatgtgttt ccagccacac caaaaggtgc ttgggggtgga gggctggggg catananggt 240
 cangcctcag gaagcctcaa gttccattca gctttgccac tgtacattcc ccatntttaa 300
 aaaaactgat gccttttttt tttttttttg taaaattc 338

<210> 139
 <211> 382
 <212> DNA
 <213> Homo sapien

<400> 139
 gggaatcttg gtttttggca tctggtttgc ctatagccga ggccactttg acagaacaaa 60
 gaaagggact tcgagtaaga aggtgattta cagccagcct agtgcccga gtgaaggaga 120
 attcaaacag acctcgtcat tcctggtgtg agcctggtcg gtcaccgcc tatcatctgc 180
 atttgcccta ctcaggtgct accggactct ggcccctgat gtctgtagt tccaggatg 240
 ccttatttgt cttctacacc ccacagggcc cctacttct tcggatgtgt ttttaataat 300
 gtcagctatg tgcccatcc tccttcacgc cctccctccc tttcctacca ctgctgagt 360
 gcctggaact tgtttaaagt gt 382

<210> 140
 <211> 200
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(200)
 <223> n = A,T,C or G

<400> 140
 accaaanctt ctttctgttg tgttngattt tactataggg gtttngcttn ttctaaanat 60
 acttttcatt taacancttt tgttaagtgt caggctgcac tttgctccat anaattattg 120
 ttttcacatt tcaacttgta tgtgtttgtc tcttanagca ttggtgaaat cacatatttt 180
 atattcagca taaaggagaa 200

<210> 141
 <211> 335
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(335)
 <223> n = A,T,C or G

<400> 141
 actttat tttt caaaacactc atatgttgca aaaaacacat agaaaaataa agtttggtgg 60
 ggggtgctgac taaacttcaa gtcacagact tttatgtgac agattggagc aggggtttgtt 120
 atgcatgtag agaaccctaaa ctaatttatt aaacaggata gaaacaggct gtctgggtga 180
 aatggttctg agaaccatcc aattcacctg tcagatgctg atanactagc tcttcagatg 240
 tttttctacc agttcagaga tnggttaatg actanttcca atgggggaaa agcaagatgg 300
 attcacaac caagtaattt taaacaaaga cactt 335

<210> 142
 <211> 459
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(459)
 <223> n = A,T,C or G

<400> 142
 accagggttaa tattgccaca tatatccttt ccaattgcgg gctaaacaga cgtgtattta 60
 ggggtgtttta aagacaaccc agcttaatat caagagaaat tgtgaccttt catggagtat 120
 ctgatggaga aaacactgag ttttgacaaa tcttatttta ttcagatagc agtctgatca 180
 cacatgggtcc aacaacactc aaataataaa tcaaatatna tcagatgtta aagattggtc 240
 ttcaaacatc atagccaatg atgccccgct tgcctataat ctctccgaca taaaaccaca 300
 tcaaacactc agtggccacc aaaccattca gcacagcttc cttaactgtg agctgtttga 360
 agctaccagt ctgagcacta ttgactatnt ttttcangct ctgaatagct ctagggatct 420
 cagcanggggt gggaggaacc agctcaacct tggcgtaant 459

<210> 143
 <211> 140
 <212> DNA
 <213> Homo sapien

<400> 143
 acatttcctt ccaccaagtc aggactcctg gcttctgtgg gagttcttat cacctgaggg 60
 aaatccaaac agtctctcct agaaaggaat agtgtcacca accccaccca tctccttgag 120
 accatccgac ttcctgtgt 140

<210> 144
 <211> 164
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(164)
 <223> n = A,T,C or G

<400> 144
 acttcagtaa caacatacaa taacaacatt aagtgtatat tgccatcttt gtcattttct 60
 atctatacca ctctcccttc tgaaaacaan aatcactanc caatcactta tacaaatttg 120
 aggcaattaa tccatatttg ttttcaataa ggaaaaaaag atgt 164

<210> 145
 <211> 303
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(303)
 <223> n = A,T,C or G

<400> 145
 acgtagacca tccaactttg tatttgtaat ggcaaacatc cagnagcaat tcctaaacaa 60
 actggagggt atttataccc aattatccca ttcattaaca tgccctcctc ctcaggctat 120
 gcaggacagc tatcataagt cggcccaggc atccagatac taccatttgt ataaacttca 180
 gtaggggagt ccattccaagt gacaggtcta atcaaaggag gaaatggaac ataagcccag 240
 tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgccgtgg tgattaccat 300
 caa 303

<210> 146
 <211> 327
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(327)
 <223> n = A,T,C or G

<400> 146
 actgcagctc aattagaagt ggtctctgac tttcatcanc ttctccctgg gctccatgac 60
 actggcctgg agtgactcat tgctctggtt gggtgagaga gctcctttgc caacaggcct 120
 ccaagtcagg gctgggattt gtttcccttc cacattctag caacaatatg ctggccactt 180
 cctgaacagg gaggtggga ggagccagca tggaacaagc tgccactttc taaagtagcc 240
 agacttgccc ctgggcctgt cacacctact gatgacctc tgtgcctgca ggatggaatg 300
 taggggtgag ctgtgtgact ctatggt 327

<210> 147
 <211> 173
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(173)
 <223> n = A,T,C or G

<400> 147
 acattgtttt tttagataa agcattgana gagctctcct taacgtgaca caatggaagg 60
 actggaacac ataccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt 120
 atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gtt 173

<210> 148

<211> 477
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(477)
<223> n = A,T,C or G

<400> 148
acaaccactt tatctcatcg aatttttaac ccaaactcac tcaactgtgcc tttctatcct 60
atgggatata ttatttgatg ctccatttca tcacacatat atgaataata cactcatact 120
gccctactac ctgctgcaat aatcacattc ccttcctgtc ctgaccctga agccattggg 180
gtggtcctag tggccatcag tccangcctg caccttgagc ccttgagctc cattgtcac 240
nccancccac ctcaccgacc ccatcctctt acacagctac ctccctgtgc tctaacccca 300
tagattatnt ccaaattcag tcaattaagt tactattaac actctaccg acatgtccag 360
caccactggt aagccttctc cagccaacac acacacacac acacncacac acacacatat 420
ccaggcacag gctacctcat cttcacaatc acccctttaa ttaccatgct atgggtgg 477

<210> 149
<211> 207
<212> DNA
<213> Homo sapien

<400> 149
acagttgtat tataatatca agaaataaac ttgcaatgag agcatttaag agggaagaac 60
taacgtatnt tagagagcca aggaagggtt ctgtggggag tgggatgtaa ggtggggcct 120
gatgataaat aagagtcagc caggtaagtg ggtggtgtgg tatgggcaca gtgaagaaca 180
tttcaggcag aggggaacagc agtgaaa 207

<210> 150
<211> 111
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(111)
<223> n = A,T,C or G

<400> 150
accttgatnt cattgctgct ctgatggaaa cccaactatc taatttagct aaaacatggg 60
cacttaaatg tggtcagtgt ttggacttgt taactantgg catctttggg t 111

<210> 151
<211> 196
<212> DNA
<213> Homo sapien

<400> 151
agcgcggcag gtcattattga acattccaga tacctatcat tactcgatgc tgttgataac 60
agcaagatgg ctttgaactc agggtcacca ccagctattg gaccttacta tgaaaaccat 120
ggataccaac cggaaaaccc ctatcccgca cagccactg tggccccac tgtctacgag 180
gtgcatccgg ctcagt 196

<210> 152
<211> 132
<212> DNA

<213> Homo sapien

<400> 152

acagcacttt	cacatgtaag	aagggagaaa	ttcctaaatg	taggagaaag	ataacagAAC	60
cttcccttt	tcatttagtg	gtggaaacct	gatgctttat	gttgacagga	atagaaccag	120
gagggagttt	gt					132

<210> 153

<211> 285

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(285)

<223> n = A,T,C or G

<400> 153

acaanaccca	nganaggcca	ctggccgtgg	tgctcatggc	tccaaacatg	aaagtgtcag	60
cttctgctct	tatgtctca	tctgacaact	ctttaccatt	tttatcctcg	ctcagcagga	120
gcacatcaat	aaagtccaaa	gtcttgact	tggccttggc	ttggaggaag	tcataaacac	180
cctggctagt	gaggggtcgg	cgccgctcct	ggatgacggc	atctgtgaag	tcgtgcacca	240
gtctgcaggc	cctgtggaag	cgccgtccac	acggagtnag	gaatt		285

<210> 154

<211> 333

<212> DNA

<213> Homo sapien

<400> 154

accacagtcc	tggtgggcca	gggcttcatg	accctttctg	tgaaaagcca	tattatcacc	60
accccaaatt	tttccttaaa	tatctttaac	tgaaggggtc	agcctcttga	ctgcaaagac	120
cctaagccgg	ttacacagct	aactcccact	ggccctgatt	tgtgaaattg	ctgctgcctg	180
attggcacag	gagtgcgaag	tggtcagctc	ccctcctcgg	tggaacgaga	ctctgatttg	240
agtttcacaa	attctcgggc	cacctcgta	ttgctcctct	gaaataaaat	ccggagaatg	300
gtcaggcctg	tctcatccat	atggatcttc	cgg			333

<210> 155

<211> 308

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(308)

<223> n = A,T,C or G

<400> 155

actggaaata	ataaaaccca	catcacagtg	ttgtgtcaaa	gatcatcagg	gcatggatgg	60
gaaagtgtt	tggaactgt	aaagtgccta	acacatgatc	gatgattttt	gttataatat	120
ttgaatcacg	gtgcatacaa	actctcctgc	ctgctcctcc	tgggccccag	ccccagcccc	180
atcacagctc	actgctctgt	tcatccaggc	ccagcatgta	gtggctgatt	cttcttggt	240
gcttttagcc	tccanaagtt	tctctgaagc	caaccaaacc	tctangtgta	aggcatgctg	300
gccctggt						308

<210> 156

<211> 295

<212> DNA

<213> Homo sapien

<400> 156

accttgctcg	gtgcttgga	catattagga	actcaaaata	tgagatgata	acagtgccta	60
ttattgatta	ctgagagAAC	tgtagacat	ttagttgaag	atcttctaca	caggaaactga	120
gaataggaga	ttatgtttgg	ccctcatatt	ctctctatc	ctccttgcc	cattctatgt	180
ctaataatatt	ctcaatcaaa	taaggttagc	ataatcagga	aatcgaccaa	ataccaatat	240
aaaaccagat	gtctatcctt	aagattttca	aatagaaaac	aaattaacag	actat	295

<210> 157

<211> 126

<212> DNA

<213> Homo sapien

<400> 157

acaagtttaa	atagtgtgt	cactgtgcat	gtgctgaaat	gtgaaatcca	ccacatttct	60
gaagagcaaa	acaaattctg	tcatgtaate	tctatcttgg	gtcgtgggta	tatctgtccc	120
cttagt						126

<210> 158

<211> 442

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(442)

<223> n = A,T,C or G

<400> 158

accactgggt	cttggaaca	cccacctta	atacgatgat	ttttctgtcg	tgtgaaaatg	60
aanccagcag	gctgccccta	gtcagtcctt	ccttccagag	aaaaagagat	ttgagaaagt	120
gcctgggtaa	ttcaccatta	atttcctccc	ccaaactctc	tgagtcttcc	cttaatat	180
ctggtggttc	tgaccaaagc	aggtcatggt	ttgttgagca	tttgggatcc	cagtgaagta	240
natgtttgta	gccttgcata	cttagccctt	cccacgcaca	aacggagtgg	cagagtgggtg	300
ccaaccctgt	tttcccagtc	cacgtagaca	gattcacagt	gcggaattct	ggaagctgga	360
nacagacggg	ctctttgcag	agccgggact	ctgagangga	catgagggcc	tctgcctctg	420
tggttcattct	ctgatgtcct	gt				442

<210> 159

<211> 498

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(498)

<223> n = A,T,C or G

<400> 159

acttccaggt	aacgttgttg	tttccgttga	gcctgaactg	atgggtgacg	ttgtaggttc	60
tccaacaaga	actgaggttg	cagagcgggt	agggaaagat	gctgttccag	ttgcacctgg	120
gctgctgtgg	actgttgttg	attcctcact	acggcccaag	gttgtggaac	tggcanaaag	180
gtgtgttgtt	gganttgagc	tggggcggct	gtggtaggtt	gtgggtctct	caacaggggc	240
tgctgtgggtg	ccgggagtg	aangtgttgt	gtcacttgag	cttggccagc	tctggaaagt	300
antanattct	tctgaaggc	cagcgcttgt	ggagctggca	ngggtcantg	ttgtgtgtaa	360
cgaaccagtg	ctgctgtggg	tgggtgtana	tcctccacaa	agcctgaagt	tatggtgtcn	420
tcaggtaana	atgtggtttc	agtgtccctg	ggcngctgtg	gaaggttgta	nattgtcacc	480

aagggaataa gctgtggt

498

<210> 160

<211> 380

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(380)

<223> n = A,T,C or G

<400> 160

acctgcatcc agcttccctg ccaaaactcac aaggagacat caacctctag acagggaac	60
agcttcagga tacttccagg agacagagcc accagcagca aaacaaatat tcccatgcct	120
ggagcatggc atagaggaag ctganaaatg tggggctctga ggaagccatt tgagtctggc	180
cactagacat ctcatcagcc acttgtgtga agagatgccc catgacccca gatgcctctc	240
ccacccttac ctccatctca cacacttgag ctttccactc tgtataattc taacatcctg	300
gagaaaaatg gcagtttgac cgaacctgtt cacaacgta gaggctgatt tctaacgaaa	360
cttgtagaat gaagcctgga	380

<210> 161

<211> 114

<212> DNA

<213> Homo sapien

<400> 161

actccacatc cctctgagc aggcggttgt cgttcaaggt gtatttggcc ttgcctgtca	60
cactgtccac tggcccctta tccacttggt gcttaatccc tcgaaagagc atgt	114

<210> 162

<211> 177

<212> DNA

<213> Homo sapien

<400> 162

actttctgaa tcgaatcaaa tgatacttag tgtagtttta atatcctcat atatatcaaa	60
gttttactac tctgataatt ttgtaaacca ggtaaccaga acatccagtc atacagcttt	120
tggtgatata taacttgga ataaccagc ctggtgatac ataaaactac tcaactgt	177

<210> 163

<211> 137

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(137)

<223> n = A,T,C or G

<400> 163

catttataca gacaggcgtg aagacattca cgacaaaaac gcgaaattct atcccgtgac	60
canagaaggc agctacggct actcctacat cctggcgtgg gtggccttcg cctgcacctt	120
catcagcggc atgatgt	137

<210> 164

<211> 469

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(469)

<223> n = A,T,C or G

<400> 164

```
ettatcacaa tgaatgttct cctgggcagc gttgtgatct ttgccacctt cgtgacttta      60
tgcaatgcat catgctatct catacctaat gagggagttc caggagattc aaccaggaaa      120
tgcattggatc tcaaaggaaa caaacaccca ataaactcgg agtggcagac tgacaactgt      180
gagacatgca cttgctacga aacagaaatt tcatgttgca cccttgtttc tacacctgtg      240
ggttatgaca aagacaactg ccaaagaatc ttcaagaagg aggactgcaa gtatatcggt      300
gtggagaaga aggacccaaa aaagacctgt tctgtcagtg aatggataat ctaatgtgct      360
tctagtaggc acagggtccc caggccaggc ctcattctcc tctggcctct aatagtcaat      420
gattgtgtag ccattgcctat cagtaaaaag atntttgagc aaacacttt      469
```

<210> 165

<211> 195

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(195)

<223> n = A,T,C or G

<400> 165

```
acagtttttt atatatatcg acattgccgg cacttggtgt cagtttcata aagctgggtg      60
atccgctgtc atccactatt ccttggttag agtaaaaatt attcttatag cccatgtccc      120
tgcaggccgc ccgcccgtag ttctcgttcc agtcgtcttg gcacacaggg tgccaggact      180
tcctctgaga tgagt      195
```

<210> 166

<211> 383

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(383)

<223> n = A,T,C or G

<400> 166

```
acatcttagt agtgtggcac atcagggggc catcagggtc acagtcactc atagcctcgc      60
cgaggtcgga gtccacacca ccggtgtagg tgtgctcaat cttgggcttg gcgcccacct      120
ttggagaagg gatatgctgc acacacatgt ccacaaagcc tgtgaactcg ccaaagaatt      180
tttgagacc agcctgagca aggggaggat gttcagcttc agctcctcct tcgtcagggtg      240
gatgccaacc tcgtctangg tccgtgggaa gctgggtgcc acntcaccta caacctgggc      300
gangatctta taaagaggct ccnagataaa ctccacgaaa cttctctggg agctgctagt      360
nggggccttt ttggtgaact ttc      383
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<210> 167

<211> 247

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature
 <222> (1)...(247)
 <223> n = A,T,C or G

<400> 167
 acagagccag accttgGCCa taaatgaanc agagattaag actaaacccc aagtcganat 60
 tggagcagaa actggagcaa gaagtgggcc tggggctgaa gtagagacca aggccactgc 120
 tatanccata cacagagcca actctcaggc caaggcnatg gttggggcag anccagagac 180
 tcaatctgan tccaaagtgg tggctggaac actggtcatg acanaggcag tgactctgac 240
 tgangtc 247

<210> 168
 <211> 273
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(273)
 <223> n = A,T,C or G

<400> 168
 acttctaagt tttctagaag tggaaggatt gtantcatcc tgaaaatggg tttacttcaa 60
 aatccctcan ccttgttctt cacnactgtc tatactgana gtgtcatggt tccacaaagg 120
 gctgacacct gagcctgnat tttcactcat ccctgagaag ccctttccag taggggtgggc 180
 aattccaac ttccttgcca caagcttccc aggttttctc ccctggaaaa ctccagcttg 240
 agtcccagat acactcatgg gctgccttgg gca 273

<210> 169
 <211> 431
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(431)
 <223> n = A,T,C or G

<400> 169
 acagccttgg cttccccaaa ctccacagtc tcagtgcaga aagatcatct tccagcagtc 60
 agctcagacc aggggtcaaag gatgtgacat caacagtttc tggtttcaga acaggttcta 120
 ctactgtcaa atgaccccc atacttcctc aaaggctgtg gtaagttttg cacaggtgag 180
 ggcagcagaa aggggggtant tactgatgga caccatcttc tctgtatact ccacactgac 240
 cttgcatggt gcaaaggccc ctaccacaaa aacaatagga tcaactgctg gcaccagctc 300
 acgcacatca ctgacaaccg ggatggaaaa agaantgcca actttcatac atccaactgg 360
 aaagtgatct gatactggat tcttaattac cttcaaaaagc ttctgggggc catcagctgc 420
 tcgaacactg a 431

<210> 170
 <211> 266
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(266)
 <223> n = A,T,C or G

<400> 170

```

acctgtgggc tgggctgtta tgctgtgcc ggctgtgaa agggagttca gaggtggagc      60
tcaaggagct ctgcaggcat ttgccaanc ctctccanag canagggagc aacctacact      120
ccccgctaga aagacaccag attggagtcc tgggaggggg agttgggggtg ggcatttgat      180
gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg anattggcct      240
tcaaagctag gggctctggca ggtgga                                         266

```

<210> 171

<211> 1248

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(1248)

<223> n = A,T,C or G

<400> 171

```

ggcagccaaa tcataaacgg cgaggactgc agcccgact cgcagccctg gcaggcggca      60
ctggctcatgg aaaacgaatt gttctgctcg ggcgtcctgg tgcattccga gtgggtgctg      120
tcagccgcac actgtttcca gaagtgagtg cagagctcct acaccatcgg gctgggcctg      180
cacagtcttg aggccgacca agagccaggg agccagatgg tggaggccag cctctccgta      240
cggcaccag agtacaacag acccttctgc gctaacgacc tcatgctcat caagttggac      300
gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgcctacc      360
gcggggaaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc      420
gtgctgcagt gcgtgaacgt gtccgtggtg tctgaggagg tctgcagtaa gctctatgac      480
ccgctgtacc accccagcat gttctgcgcc ggccggaggc aagaccagaa ggactcctgc      540
aacggtgact ctggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtcttcc      600
ggaaaagccc cgtgtggcca agttggcgtg ccaggtgtct acaccaacct ctgcaaattc      660
actgagtgga tagagaaaac cgtccaggcc agttaactct ggggactggg aaccatgaa      720
attgaccccc aaatacatcc tgcggaagga attcaggaat atctgttccc agccctcct      780
ccctcaggcc caggagtcca ggcccccagc cctcctccc tcaaaccaag ggtacagatc      840
cccagccct cctccctcag acccaggagt ccagacccc cagccctcc tccctcagac      900
ccaggagtcc agccctcct cctcagacc caggagtcca gacccccag cccctcctcc      960
ctcagaccca ggggtccagg ccccaacc cctcctccc agactcagag gtccaagccc      1020
ccaaccntc attccccaga cccagaggtc caggtcccag cccctntcc ctcagaccca      1080
gcggtccaat gccacctaga ctntccctgt acacagtgc cccttggtgg acgttgacct      1140
aaccttacca gttggttttt catttttngt ccctttcccc tagatccaga aataaagttt      1200
aagagaagng caaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa                    1248

```

<210> 172

<211> 159

<212> PRT

<213> Homo sapien

<220>

<221> VARIANT

<222> (1)...(159)

<223> Xaa = Any Amino Acid

<400> 172

```

Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro
 1              5              10              15
Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser
 20              25              30
Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr
 35              40              45
Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly

```

50	55	60
Arg Met Pro Thr Val	Leu Gln Cys Val Asn Val	Ser Val Val Ser Glu
65	70	75
Glu Val Cys Ser Lys	Leu Tyr Asp Pro Leu Tyr	His Pro Ser Met Phe
85	90	95
Cys Ala Gly Gly Gln	Xaa Gln Xaa Asp Ser Cys	Asn Gly Asp Ser
100	105	110
Gly Gly Pro Leu Ile	Cys Asn Gly Tyr Leu Gln	Gly Leu Val Ser Phe
115	120	125
Gly Lys Ala Pro Cys	Gly Gln Val Gly Val Pro	Gly Val Tyr Thr Asn
130	135	140
Leu Cys Lys Phe Thr	Glu Trp Ile Glu Lys Thr	Val Gln Ala Ser
145	150	155

<210> 173
 <211> 1265
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(1265)
 <223> n = A,T,C or G

<400> 173	
ggcagccgc actgcagcc ctggcaggcg gcaactggtca tggaaaacga attgttctgc	60
tcgggcgtcc tgggtcatcc gcagtgggtg ctgtcagccg cacactgttt ccagaactcc	120
tacaccatcg ggctgggcct gcacagtctt gaggccgacc aagagccagg gagccagatg	180
gtggaggcca gcctctccgt acggcaccca gactacaaca gacccttgct cgctaacgac	240
ctcatgctca tcaagtggga cgaatccgtg tccgagtctg acaccatccg gagcatcagc	300
attgcttcgc agtgcctac cgcggggaac tcttgctcg tttctggctg gggctctgctg	360
gcgaacggtg agctcacggg tgtgtgtctg cctcttcaa ggaggtcctc tgcccagtcg	420
cgggggctga cccagagctc tgcgtcccag gcagaatgcc taccgtgctg cagtgcgtga	480
acgtgtcggt ggtgtctgag gaggtctgca gtaagctcta tgaccgcctg taccaccca	540
gcatgttctg cgcgcgcgga gggcaagacc agaaggactc ctgcaacggt gactctgggg	600
ggccctgat ctgcaacggg tacttgagg gccttgctg tttcgaaaa gcccgtgtg	660
gccaagttgg cgtgccagggt gtctacacca acctctgcaa attcactgag tggatagaga	720
aaaccgtcca ggccagttaa ctctggggac tgggaaccca tgaaattgac ccccaaatac	780
atcctgcgga aggaattcag gaatatctgt tcccagcccc tctcctcaga ggcccaggag	840
tccaggcccc cagccctcc tccctcaaac caagggtaca gatccccagc cctcctccc	900
tcagacccag gagtccagac cccccagccc ctctcctc agacccagga gtccagcccc	960
tcctccntca gaccagagg tccagacccc ccagccctc ctccctcaga cccaggggtt	1020
gaggcccca acccctcctc cttcagagtc agaggtccaa gcccacaacc cctcgttccc	1080
cagacccaga ggttnnaggtc ccagccctc ttccntcaga cccagnngtc caatgccacc	1140
tagatatttc ctgnacacag tgccccttg tgganngttg acccaacctt accagttggt	1200
ttttcatttt tngtcccttt cccctagatc cagaaataaa gtttaagaga ngngcaaaaa	1260
aaaaa	1265

<210> 174
 <211> 1459
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(1459)
 <223> n = A,T,C or G

<400> 174

```

ggtcagccgc acactgtttc cagaagtgag tgcagagctc ctacaccatc gggctgggccc 60
tgcacagtct tgaggccgac caagagccag ggagccagat ggtggaggcc agcctctccg 120
tacggcacc caggtacaac agacccttgc tcgctaacga cctcatgctc atcaagttgg 180
acgaatccgt gtccgagtct gacaccatcc ggagcatcag cattgcttcg cagtgcctta 240
ccgcggggaa ctcttgccctc gtttcttggt ggggtctgct ggcgaacggg gagctcacgg 300
gtgtgtgtct gccctcttca aggaggtcct ctgccagctc gcgggggctg acccagagct 360
ctgcgtccca ggcagaatgc ctaccgtgct gcagtgcgtg aacgtgtcgg tgggtgtctga 420
ngaggtctgc antaagctct atgacccgct gtaccacccc ancatgttct gcgccggcgg 480
agggcaagac cagaaggact cctgcaacgt gagagagggg aaaggggagg gcaggcgact 540
caggggaagg tggagaagg ggagacagag acacacaggg ccgcatggcg agatgcagag 600
atggagagac acacagggag acagtgacaa cttagagagag aaactgagag aaacagagaa 660
ataaacacag gaataaagag aagcaaaagg agagagaaac agaaacagac atggggaggc 720
agaaacacac acacatagaa atgcagttga ccttccaaca gcatggggcc tgagggcggg 780
gacctccacc caatagaaaa tctctttata acttttgact ccccaaaaac ctgactagaa 840
atagcctact gttgacgggg agccttacca ataacataaa tagtcgattt atgcatacgt 900
tttatgcatt catgatatac ctttgttggg attttttgat atttctaagc tacacagttc 960
gtctgtgaat ttttttaaat tgttgcaact ctctaaaaat ttttctgatg tgtttattga 1020
aaaaatccaa gtataagtg acttggtgcat tcaaacagg gttgttcaag ggtcaactgt 1080
gtaccagag ggaacagtg acacagattc atagaggtga aacacgaaga gaaacaggaa 1140
aatcaagac tctacaaaga ggctgggcag ggtggctcat gcctgtaac ccagcacttt 1200
gggagggcag gcaggcagat cacttgaggt aaggagttca agaccagcct ggccaaaatg 1260
gtgaaatcct gtctgtacta aaaatacaaa agttagctgg atatggtggc aggcgcctgt 1320
aatccagct acttgggagg ctgaggcagg agaattgctt gaatatggga ggcagaggtt 1380
gaagtgaagt gagatcacac cactatactc cagctggggc aacagagtaa gactctgtct 1440
caaaaaaaaa aaaaaaaaaa

```

<210> 175

<211> 1167

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(1167)

<223> n = A,T,C or G

<400> 175

```

gcgcagccct ggcaggcggc actgggtcatg gaaaacgaat tgttctgctc gggcgtcctg 60
gtgcatccgc agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg 120
ctgggcctgc acagtcttga ggccgaccaa gagccaggga gccagatggg ggaggccagc 180
ctctccgtac ggcacccaga gtacaacaga ctcttgctcg ctaacgacct catgctcacc 240
aagtggagc aatccgtgtc cgagtctgac accatccgga gcacagcat tgcttcgcag 300
tgccctaccg cggggaactc ttgcctcgtn tctggctggg gtctgctggc gaacggcaga 360
atgcctaccg tgctgcactg cgtgaacgtg tcgggtggtg ctgaggangt ctgcagtaag 420
ctctatgacc cgctgtacca cccagcatg ttctgcgccg gcggagggca agaccagaag 480
gactcctgca acggtgactc tggggggccc ctgatctgca acgggtactt gcagggcctt 540
gtgtctttcg gaaaagcccc gtgtggccaa cttggcgtgc cagggtgtct caccaacctc 600
tgcaaatcca ctgagtggat agagaaaacc gtcagncca gttactctg gggactggga 660
acctatgaaa ttgaccccca aatacatcct gcggaangaa ttcaggaata tctgttccca 720
gccccctctc cctcaggccc aggagtcag gccccagcc cctcctccct caaaccagg 780
gtacagatcc ccagccctc ctccctcaga cccaggagtc cagaccccc agccccctnt 840
cctcagacc caggagtcca gccccctc cctcagacgc aggagtcag accccccagc 900
cctcctccg tcagaccag ggtgcaggc ccccaacccc tctcctntca gagtgcagg 960
tccaagcccc caaccctcg tccccagac ccagaggtnc aggtcccagc cctcctccc 1020
tcagaccag cgggtccaat ccacctagan tntccctgta cacagtgcct ccttgtggca 1080
ngttgacca acctaccag ttggtttttc attttttgtc cctttccct agatccagaa 1140
ataaagtnta agagaagcgc aaaaaaa

```

1167

<210> 176
 <211> 205
 <212> PRT
 <213> Homo sapien

<220>
 <221> VARIANT
 <222> (1)...(205)
 <223> Xaa = Any Amino Acid

<400> 176
 Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
 1 5 10 15
 Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
 20 25 30
 Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
 35 40 45
 Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Leu Leu Leu
 50 55 60
 Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
 65 70 75 80
 Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
 85 90 95
 Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met
 100 105 110
 Pro Thr Val Leu His Cys Val Asn Val Ser Val Val Ser Glu Xaa Val
 115 120 125
 Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala
 130 135 140
 Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly
 145 150 155 160
 Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys
 165 170 175
 Ala Pro Cys Gly Gln Leu Gly Val Pro Gly Val Tyr Thr Asn Leu Cys
 180 185 190
 Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Xaa Ser
 195 200 205

<210> 177
 <211> 1119
 <212> DNA
 <213> Homo sapien

<400> 177
 gcgcactcgc agccctggca ggcggcactg gtcattggaaa acgaattggt ctgctcgggc 60
 gtcctggtgc atccgcagtg ggtgctgtca gccgcacact gtttcagaa ctectacacc 120
 atcgggctgg gcctgcacag tcttgaggcc gaccaagagc caggagacca gatggtggag 180
 gccagcctct ccgtacggca cccagagtac aacagaccct tgctcgctaa cgacctcatg 240
 ctcatcaagt tggacgaatc cgtgtccgag tctgacacca tccggagcat cagcattgct 300
 tcgcagtgcc ctaccgcggg gaactcttgc ctcgtttctg gctggggtct gctggcgaac 360
 gatgctgtga ttgccatcca gtcccagact gtgggaggtc gggagtgtga gaagctttcc 420
 caaccttggc aggggtgtac catttcggca acttccagtg caaggacgtc ctgctgcac 480
 ctactgggt gctcactact gctcactgca tcaccggaa cactgtgatc aactagccag 540
 caccatagtt ctccgaagtc agactatcat gattactgtg ttgactgtgc tgtctattgt 600
 actaaccatg ccgatgttta ggtgaaatta gcgtcacttg gcctcaacca tcttggtatc 660
 cagttatcct cactgaattg agatttcctg cttcagtgtc agccattccc acataatttc 720
 tgacctacag aggtgaggga tcatatagct cttcaaggat gctggtactc ccctcacaaa 780

```

ttcatttctc ctgtttagt gaaaggtgag ccctctggag cctcccaggg tgggtgtgca      840
ggtcacaatg atgaatgtat gatcgtgttc ccattaccca aagcctttaa atccctcatg      900
ctcagtacac cagggcaggt ctagcatttc ttcatttagt gtatgctgtc cattcatgca      960
accacctcag gactcctgga ttctctgcct agttgagctc ctgcatgctg cctccttggg     1020
gaggtgaggg agagggccca tggttcaatg ggatctgtgc agttgtaaca cattaggtgc     1080
ttaataaaca gaagctgtga tgtaaaaaa aaaaaaaaaa     1119

```

<210> 178

<211> 164

<212> PRT

<213> Homo sapien

<220>

<221> VARIANT

<222> (1) ... (164)

<223> Xaa = Any Amino Acid

<400> 178

```

Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
 1              5              10              15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
 20              25              30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
 35              40              45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu
 50              55              60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
 65              70              75              80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
 85              90              95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val
100              105              110
Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu
115              120              125
Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg
130              135              140
Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Thr Ala Ser
145              150              155              160
Pro Gly Thr Leu

```

<210> 179

<211> 250

<212> DNA

<213> Homo sapien

<400> 179

```

ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct      60
ccagctgccc cgggccgggg gatgcgaggg tcggagcacc cttgccccgc tgtgattgct      120
gccaggcact gttcatctca gcttttctgt ccctttgctc ccggcaagcg cttctgctga      180
aagttcatat ctggagcctg atgtcttaac gaataaaggt cccatgctcc acccgaaaaa      240
aaaaaaaaa                                     250

```

<210> 180

<211> 202

<212> DNA

<213> Homo sapien

<400> 180
 actagtccag tgtgggtggaa ttccattgtg ttggggcccaa cacaatgggt acctttaaca 60
 tcaccagac cccgcccctg cccgtgcccc acgctgctgc taacgacagt atgatgctta 120
 ctctgctact cggaaactat ttttatgtaa ttaatgtatg ctttcttggt tataaatgcc 180
 tgatttataaa aaaaaaaaaa aa 202

<210> 181
 <211> 558
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (558)
 <223> n = A,T,C or G

<400> 181
 tccytttgkt naggttttkg agacamccck agacctwaan ctgtgtcaca gacttcyngg 60
 aatgttttagg cagtgtctagt aatttcytcg taatgattct gttattactt tcctnattct 120
 ttattcctct ttcttctgaa gattaatgaa gttgaaaatt gaggtggata aatacaaaaa 180
 ggtagtgtga tagtataagt atctaagtgc agatgaaagt gtgttatata tatccattca 240
 aaattatgca agttagtaat tactcagggt taactaaatt actttaatat gctgttgaaac 300
 ctactctgtt ccttggttag aaaaaattat aaacaggact ttgttagttt gggaagccaa 360
 attgataata ttctatgttc taaaagttgg gctatacata aattattaag aaatatggaw 420
 ttttattccc aggaatatgg kgttcatttt atgaatatta cscrggatag awgtwtgagt 480
 aaaaycagtt ttggtwaata ygtwaatatg tcmtaaataa acaakgcttt gacttatctc 540
 caaaaaaaaa aaaaaaaaaa 558

<210> 182
 <211> 479
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (479)
 <223> n = A,T,C or G

<400> 182
 acagggwttk grggatgcta agsccccrga rwtggtttga tccaaccctg gcttwttttc 60
 agaggggaaa atggggccta gaagttacag mscatytagy tgggtgcgmtg gcacccctgg 120
 cstcacacag astcccaggt agctgggact acaggcacac agtcactgaa gcaggccctg 180
 ttwgcaattc acgttgccac ctccaactta aacattcttc atatgtgatg tccttagtca 240
 ctaaggttaa actttcccac ccagaaaagg caacttagat aaaatcttag agtactttca 300
 tactmttcta agtctctctc cagcctcact kkgagtcctm cytggggggt gataggaant 360
 ntctcttggc tttctcaata aartctctat ycatctcatg ttttaatttgg tacgcataa 420
 awtgstgata aaattaaaat gttctggtty mactttaaaa aaaaaaaaaa aaaaaaaaaa 479

<210> 183
 <211> 384
 <212> DNA
 <213> Homo sapien

<400> 183
 aggcggggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc 60
 agtaccagta ccaataacag tgccagtgcc agtgccagca ccagtgggtg cttcagtgtc 120
 ggtgccagcc tgaccgccac tctcacattt gggctcttcg ctggccttgg tggagctggt 180
 gccagcacca gtggcagctc tgggtgcctgt ggtttctcct acaagtgaga ttttagatat 240

tgtaatacct gccagtcttt ctcttcaagc caggggtgcat cctcagaaac ctactcaaca 300
cagcactcta ggcagccact atcaatcaat tgaagttgac actctgcatt aratctattt 360
gccatttcaa aaaaaaaaaa aaaa 384

<210> 184

<211> 496

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(496)

<223> n = A,T,C or G

<400> 184

accgaattgg gaccgctggc ttataagcga tcatgtyynt ccrgtatkac ctcaacgagc 60
agggagatcg agtctatacg ctgaagaaat ttgacccgat gggacaacag acctgctcag 120
cccatectgc tcggttctcc ccagatgaca aatactctsg acaccgaatc accatcaaga 180
aacgcttcaa ggtgctcatg acccagcaac cgcgcctgt cctctgaggg tcccttaaac 240
tgatgtcttt tctgccacct gttacccctc ggagactccg taaccaaact ctccggactg 300
tgagccctga tgcctttttg ccagccatac tctttggcat ccagtctctc gtggcgattg 360
attatgcttg tgtgaggcaa tcatggtggc atcacccata aagggaacac atttgacttt 420
tttttctcat attttaaat actacmagaw tattwmagaw waaatgawtt gaaaaactst 480
taaaaaaaaa aaaaaa 496

<210> 185

<211> 384

<212> DNA

<213> Homo sapien

<400> 185

gctggtagcc tatggcgkgg cccacggagg ggctcctgag gccacggrac agtgacttcc 60
caagtatcyt gcgscgctc ttctaccgct cctacctgca gatcttcggg cagattcccc 120
aggaggacat ggacgtggcc ctcatggagc acagcaactg ytcgtcggag cccggcttct 180
gggcacaccc tcctggggcc caggcgggca cctgcgtctc ccagtatgcc aactggctgg 240
tgggtgctgt cctcgtcatc ttctgctcgt tggccaacat cctgctggtc aacttgctca 300
ttgccatgtt cagttacaca ttccggcaaag tacagggcaa cagcgatctc tactgggaag 360
gcgcagcgtt accgcctcat ccgg 384

<210> 186

<211> 577

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(577)

<223> n = A,T,C or G

<400> 186

gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggccctctcg ttcataccgc 60
tnccatcgct atactgtagg tttgccacca cytcctggca tcttggggcg gcntaatatt 120
ccaggaaact ctcaatcaag tcaccgtcga tgaaacctgt gggctggttc tgtcttcgcg 180
tcggtgtgaa aggatctccc agaaggagtg ctcgatcttc ccacacttt tgatgacttt 240
attgagtcga ttctgcatgt ccagcaggag gttgtaccag ctctctgaca gtgaggtcac 300
cagccctatc atgccgttga mcgtgccgaa garcaccgag ccttgtgtgg gggkkgaagt 360
ctcaccacaga ttctgcatta ccagagagcc gtggcaaaaag acattgacaa actcgccccag 420
gtggaaaaag amcamctcct ggargtgctn gccgctctc gtcmgttggt gccagcgctw 480

```

tccttttgac acacaaacaa gttaaaggca ttttcagccc ccagaaantt gtcacatcc 540
aagatntcgc acagcactna tccagttggg attaaat 577

```

```

<210> 187
<211> 534
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(534)
<223> n = A,T,C or G

```

```

<400> 187
aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgstg agaatycatw 60
actkggaaaa gmaacattaa agcctggaca ctgggtattaa aattcacaat atgcaacact 120
ttaaacagtg tgtcaatctg ctcccyynac tttgtcatca ccagtctggg aakaagggtg 180
tgccctattc acacctgtta aaagggcgct aagcattttt gattcaacat cttttttttt 240
gacacaagtc cgaaaaaagc aaaagtaaac agttatyaat ttgttagcca attcactttc 300
ttcatgggac agagccatyt gatttaaaaa gcaaatgca taatattgag ctttygggagc 360
tgatatttga gcggaagagt agcctttcta cttcaccaga cacaactccc tttcatattg 420
ggatgttnac naaagtwatg tctctwacag atgggatgct tttgtggcaa ttctgttctg 480
aggatctccc agtttattta ccacttgac aagaaggcgt tttcttcctc agg 534

```

```

<210> 188
<211> 761
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(761)
<223> n = A,T,C or G

```

```

<400> 188
agaaaccagt atctctnaaa acaacctctc ataccttggt gacctaatth ttgtgtgcgtg 60
tgtgtgtgcg cgcataattat atagacaggc acatcttttt tactttttgta aaagccttatg 120
cctctttggg atctatatct gtgaaagttt taatgatctg ccataatgct ttggggacct 180
ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcaa tctagttngt 240
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc ctkgackarg 300
ggggacaaaag aaaagcaaaa ctgamcataa raaacaatwa cctgggtgaga arttgcataa 360
acagaaatwr ggtagtatat tgaarnacag catcattaaa rmgttwtktt wttctccctt 420
gcaaaaaaca tgtacngact tcccgttgag taatgccaaag ttgttttttt tatnataaaa 480
cttgcccttc attacatggt tnaaagtggg gtgggtgggc aaaatattga aatgatggaa 540
ctgactgata aagctgtaca aataagcagt gtgcctaaca agcaacacag taatgttgac 600
atgcttaatt cacaagtgt aatttcatta taaatgtttg ctaaaataca ctttgaacta 660
ttttctgtgn ttcccagagc tgagatntta gattttatgt agtatnaagt gaaaaantac 720
gaaaataata acattgaaga aaananaaaa aaanaaaaaa a 761

```

```

<210> 189
<211> 482
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(482)
<223> n = A,T,C or G

```

<400> 189

tttttttttt tttgccgatn ctactatntt attgcaggan gtgggggtgt atgcaccgca	60
caccggggct atnagaagca agaaggaagg agggagggca cagccccttg ctgagcaaca	120
aagccgcttg ctgccttctc tgtctgtctc ctggtgcagg cacatgggga gaccttcccc	180
aaggcagggg ccaccagtcc aggggtggga atacaggggg tgggagtgtg gcataagaag	240
tgataggcac aggccacccg gtacagaccc ctggtctctt gacaggtnga ttctgaccag	300
gtcattgtgc cctgcccagg cacagcgtn atctggaaaa gacagaatgc ttctcttttc	360
aaatttggt ngctatngaa ngggcanttt tccaantng gctnggtctt ggtacncttg	420
gttcggccca gctcncgtc caaaaantat tcacccnct ccnaattgt tgcnggnccc	480
cc	482

<210> 190

<211> 471

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(471)

<223> n = A,T,C or G

<400> 190

tttttttttt ttttaaaaca gtttttcaca aaaaaattta ttagaagaat agtggttttg	60
aaaactctcg catccagtga gaactacat acaccacatt acagctngga atgtntctca	120
aatgtctggt caaatgatac aatggaacca ttcaatctta cacatgcacg aaagaacaag	180
cgcttttgac atacaatgca caaaaaaaaa aggggggggg gaccacatgg attaaaattt	240
taagtactca tcacatacat taagacacag ttctagtcca gtcaaaaatc agaactgcnt	300
tgaaaaattt catgtatgca atccaaccaa agaacttnat tggatgatcat gantnctcta	360
ctacatcnac cttgatcatt gccaggaacn aaaagttnaa ancacnngt acaaaaaanaa	420
tctgtaattn anttcaacct ccgtacngaa aaatnttnt tatacactcc c	471

<210> 191

<211> 402

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(402)

<223> n = A,T,C or G

<400> 191

gagggttgga aggtctgttc tastgtggm ctgttcagcc accaactcta acaagttgct	60
gtcttccact cactgtctgt aagcttttta acccagacwg tatcttcata aatagaacaa	120
attcttcacc agtcacatct tctaggacct ttttggttc agttagtata agctcttcca	180
cttcctttgt taagacttca tctggtaaag tcttaagttt tgtagaaagg aattyaattg	240
ctcgttctct aacaatgtcc tctccttgaa gtatttggt gaacaaccca cctaaagtcc	300
ctttgtgcat ccattttaaa tatacttaat agggcattgk tncactaggt taaattctgc	360
aagagtcac tgtctgcaaa agttgcgtta gtatatctgc ca	402

<210> 192

<211> 601

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (601)

<223> n = A,T,C or G

<400> 192

gagctcggat	ccaataatct	ttgtctgagg	gcagcacaca	tatncagtgc	catggnaact	60
ggctctaccc	acatgggagc	agcatgccgt	agntatataa	ggtcattccc	tgagtcagac	120
atgcytyttt	gaytaccgtg	tgccaagtgc	tggtgattct	yaacacacyt	ccatcccyt	180
cttttgtgga	aaaactggca	cttktctgga	actagcarga	catcacttac	aaattcacc	240
acgagacact	tgaaagggtg	aacaaagcga	ytcttgcat	gctttttgtc	cctccggcac	300
cagttgtcaa	tactaaccg	ctggtttgcc	tccatcacat	ttgtgatctg	tagctctgga	360
tacatctcct	gacagtactg	aagaacttct	tcttttggtt	caaaagcarg	tcttgggtgc	420
tggtggatca	ggttcccat	tcccagtcy	aatgttcaca	tggtcatatt	wacttccac	480
aaaacattgc	gatttgaggc	tcagcaacag	caaatcctgt	tccggcattg	gctgcaagag	540
cctcgatgta	gccggccagc	gccaaaggcag	gcgcggtgag	ccccaccagc	agcagaagca	600
g						601

<210> 193

<211> 608

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (608)

<223> n = A,T,C or G

<400> 193

atacagccca	natcccacca	cgaagatg	cttggtgact	gagaacctga	tgccggtcact	60
ggctccgctg	tagccccagc	gactctccac	ctgctggaag	cgggtgatgc	tgcaactcytt	120
cccaacgcag	gcagmagcgg	gsccggtcaa	tgaactccay	tcgtggcctg	gggtkgacgg	180
tkaagtgcag	gaagaggctg	accacctcgc	gggtccaccag	gatgcccag	tggtgcccggac	240
ctgcagcgaa	actcctcgat	ggatcatgagc	gggaagcgaa	tgaggcccag	ggccttgccc	300
agaaccttcc	gcctgttctc	tggtcgccacc	tgagctgct	gccgctgaca	ctcggcctcg	360
gaccagcgga	caaacggcrt	tgaacagccg	cacctcacgg	atgcccagtg	tgctcgcgctc	420
caggammgsc	accagcgtgt	ccaggtcaat	gtcgggtgaag	ccctccgcgg	gtrattggcgt	480
ctgcagtgtt	tttgcgatg	ttctccaggc	acaggtggc	cagctgcggt	tcattcgaaga	540
gtcgcgcctg	cgtgagcagc	atgaaggcgt	tgctcggtcg	cagttcttct	tcaggaactc	600
cacgcaat						608

<210> 194

<211> 392

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (392)

<223> n = A,T,C or G

<400> 194

gaacggctgg	acctgacctc	gcattgtgct	tgctggcagg	gaataccttg	gcaagcagyt	60
ccagtcgcag	cagccccaga	ccgctgccgc	ccgaagctaa	gcctgcctct	ggccttcccc	120
tccgcctcaa	tgagaacca	gtagtgggag	cactgtgttt	agagttaaga	gtgaacactg	180
tttgatttta	cttggaatt	tcctctgtta	tatagctttt	cccaatgcta	atttccaaac	240
aacaacaaca	aaataacatg	tttgctgtt	aagttgtata	aaagtaggtg	attctgtatt	300
taaagaaaat	attactgtta	catatactgc	ttgcaatttc	tgtatttatt	gktinctstgg	360
aaataaatat	agttattaaa	ggttgctcant	cc			392

<210> 195
 <211> 502
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(502)
 <223> n = A,T,C or G

<400> 195
 ccsttkgagg ggtkaggkyc cagttyccga gtggaagaaa caggccagga gaagtgcgtg 60
 ccgagctgag gcagatgttc ccacagtac cccagagccc stgggstata gtytctgacc 120
 cctcncaagg aaagaccacs ttctggggac atgggctgga gggcaggacc tagaggcacc 180
 aaggggaagg cccattccgg ggstgttccc cgaggaggaa ggggaagggc tctgtgtgcc 240
 ccccasgagg aagaggccct gagtccctgg atcagacacc ccttcacgtg tatccccaca 300
 caaatgcaag ctcaccaagg tccccctcca gtccccctcc stacaccctg amcggccact 360
 gscscacacc caccagagc acgccacccg ccatggggar tgtgctcaag gartcgcnng 420
 gcarcgtgga catctngtcc cagaaggggg cagaatctcc aatagangga ctgarcmtt 480
 gctnanaaaa aaaaaaaaaa aa 502

<210> 196
 <211> 665
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(665)
 <223> n = A,T,C or G

<400> 196
 ggttacttgg ttctattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc 60
 cctctggaag ccttgccgag agcggacttt gtaattgttg gagaataact gctgaatttt 120
 wagctgttk gagttgatts gcaccactgc acccacaact tcaatatgaa aacyawttga 180
 actwatttat tatcttgtga aaagtataac aatgaaaatt ttgttcatac tgtattkate 240
 aagtatgatg aaaagcaawa gatatatatt cttttattat gttaaattat gattgccatt 300
 attaatcggc aaaatgtgga gtgtatgttc ttttcacagt aatatatgcc ttttgtaact 360
 tcacttggtt attttattgt aaatgartta caaaattctt aatttaagar aatggatgt 420
 watatttatt tcattaattt ctttccctkt ttacgtwaat tttgaaaaga wtgcagtatt 480
 tcttgacaga aatcgatctt gatgctgtgg aagtagtttg acccacatcc ctatgagttt 540
 ttcttagaat gtataaagg ttagcccat cnaacttcaa agaaaaaat gaccacatac 600
 tttgcaatca ggctgaaatg tggcatgctn ttctaattcc aactttataa actagcaaan 660
 aagtg 665

<210> 197
 <211> 492
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(492)
 <223> n = A,T,C or G

<400> 197
 tttntttttt ttttttttgc aggaaggatt ccatttattg tggatgcatt ttcacaatat 60
 atgtttattg gagcgatcca ttatcagtga aaagatcaa gtgtttataa nttttttagg 120

```

aaggcagatt cacagaacat gctngtcngc ttgcagtttt acctcgtana gatnacagag      180
aattatagtc naaccagtaa acnaggaatt tactttttcaa aagattaaat ccaaactgaa      240
caaaattcta ccctgaaact tactccatcc aaatatggga ataanagtca gcagtgatac      300
attctcttct gaacttttaga ttttctagaa aaatatgtaa tagtgatcag gaagagctct      360
tgttcaaaaag tacaacnaag caatgttccc ttaccatagg ccttaattca aactttgatc      420
catttcactc ccatacggg agtcaatgct acctggggaca cttgtatttt gttcatnctg      480
ancntggctt aa                                                              492

```

<210> 198

<211> 478

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (478)

<223> n = A,T,C or G

<400> 198

```

tttnttttgn atttcantct gtannaanta ttttcattat gtttattana aaaatatnaa      60
tgtntccacn acaaatcatn ttacntnagt aagaggccan ctacattgta caacatacac      120
tgagtatatt ttgaaaagga caagttttaa gtanacncat attgccganc atancacatt      180
tatacatggc ttgattgata tttagcacag canaaactga gtgagttacc agaaanaaat      240
natatatgtc aatcngattt aagatacaaa acagatccta tggtagatan catcntgtag      300
gagttgtggc tttatgttta ctgaaagtca atgcagttcc tgtacaaaaga gatggccgta      360
agcattctag tacctctact ccatgggtaa gaatcgtaca cttatgttta catatgtncn      420
gggtaagaat tgtgttaagt naanttatgg agaggtccan gagaaaaatt tgatncaa      478

```

<210> 199

<211> 482

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (482)

<223> n = A,T,C or G

<400> 199

```

agtgacttgt cctccaacaa aacccttga tcaagtttgt ggcactgaca atcagaccta      60
tgctagttcc tgtcatctat tctactactaa atgcagactg gaggggacca aaaaggggca      120
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga      180
agtgattcag tttcctctac ggatgagaga ctggctcaag aatatcctca tgcagcttta      240
tgaagccnac tctgaacacg ctggttatct nagatgagaa ncagagaaat aaagtcnaga      300
aaatttacct ggangaaaag aggctttnng ctggggacca tccattgaa ccttctctta      360
anggacttta agaanaaaact accacatgtn tgtngtatcc tgggtgccngg ccgtttantg      420
aacntngacn ncacccttnt ggaatanant cttgacngcn tctgaactt gtcctctctg      480
ga

```

<210> 200

<211> 270

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (270)

<223> n = A,T,C or G

<400> 200

```
cggccgcaag tgcaactcca gctggggccg tgcggacgaa gattctgcca gcagttggtc    60
cgactgcgac gacggcggcg gcgacagtcg caggtgcagc gcgggcgcct ggggtcttgc    120
aaggctgagc tgacgccgca gaggtcgtgt cacgtccac gaccttgacg ccgtcgggga    180
cagccggaac agagcccggt gaangcggga ggcctcgggg agcccctcgg gaaggcgggc    240
ccgagagata cgcaggtgca ggtggccgcc                                270
```

<210> 201

<211> 419

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(419)

<223> n = A,T,C or G

<400> 201

```
tttttttttt ttttggaaac tactgcgagc acagcaggtc agcaacaagt ttatttttgc    60
gctagcaagg taacagggta gggcatggtt acatgttcag gtcaacttcc tttgtcgtgg    120
ttgattggtt tgtctttatg gggcggggtt ggggtagggg aaancgaagc anaantaaca    180
tggagtgggt gcaccctccc tgtagaacct gggtacnaaa gcttggggca gttcacctgg    240
tctgtgaccg tcattttctt gacatcaatg ttattagaag tcaggatata ttttagagag    300
tccactgtnt ctggagggag attaggggtt cttgccaana tccaancaa atccacntga    360
aaaagtggga tgatncangt acngaatacc ganggcatan ttctcatant cggtaggcca    419
```

<210> 202

<211> 509

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(509)

<223> n = A,T,C or G

<400> 202

```
ttnttttttt tttttttttt tttttttttt tttttttttt tttttttttt    60
tggcacttaa tccattttta tttcaaaatg tctacaaant ttnaatncnc cattatacng    120
gtnattttnc aaaatctaaa nmttattcaa atntnagcca aantccttac ncaaatnnaa    180
tacnncnaaa aatcaaaaat atacntntct ttcagcaaac ttngttacat aaattaaaaa    240
aatatatacg gctggtgttt tcaaagtaca attatcttaa cactgcaaac atnttttnnaa    300
ggaactaaaa taaaaaaaaa cactnccgca aagggttaaag ggaacaacaa attcntttta    360
caacancnnc nattataaaa atcatatctc aaatcttagg ggaatatata cttcacacng    420
ggatcttaac ttttactnca ctttggtttt ttttttanaa ccattgtntt gggcccaaca    480
caatggnaat nccnccnncn tggactagt                                509
```

<210> 203

<211> 583

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(583)

<223> n = A,T,C or G

<400> 203

tttttttttt	ttttttttga	ccccctctt	ataaaaaaca	agttaccatt	ttattttact	60
tacacatatt	tattttataa	ttggtattag	atattcaaaa	ggcagctttt	aaaatcaaac	120
taaatggaaa	ctgccttaga	tacataattc	ttaggaatta	gcttaaaatc	tgccataaag	180
gaaaatcttc	tctagctctt	ttgactgtaa	atttttgact	cttgtaaaac	atccaaattc	240
atttttcttg	tctttaaaat	tatctaattc	ttccattttt	tcctatttcc	aagtcaattt	300
gcttctctag	cctcatttcc	tagctcttat	ctactattag	taagtggctt	ttttcctaaa	360
agggaaaaca	ggaagagana	atggcacaca	aaacaaacat	tttatattca	tattttctacc	420
tacgttaata	aaatagcatt	ttgtgaagcc	agctcaaaag	aaggcttaga	tccttttatg	480
tccatttttag	tcactaaacg	atatacnaag	tgccagaatg	caaaagggtt	gtgaacattt	540
attcaaaagc	taataataaga	tatttcacat	actcatcttt	ctg		583

<210> 204

<211> 589

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(589)

<223> n = A,T,C or G

<400> 204

ttttttttnt	tttttttttt	tttttttctc	ttcttttttt	ttganaatga	ggatcgagtt	60
tttactcttc	tagatagggc	atgaagaaaa	ctcatctttc	cagcttttaa	ataacaatca	120
aatctcttat	gctatatcat	attttaagtt	aaactaatga	gtcactggct	tatcttctcc	180
tgaaggaaat	ctgttcattc	ttctcattca	tatagttata	tcaagtacta	ccttgcatat	240
tgagaggttt	ttcttctcta	tttacacata	tattttccatg	tgaatttgta	tcaaaccctt	300
attttcatgc	aaactagaaa	ataatgtntt	cttttgcata	agagaagaga	acaatatnag	360
cattacaaaa	ctgctcaaat	tgtttgttaa	gnntatccat	tataattagt	tnggcaggag	420
ctaatacaaa	tcacattttac	ngacnagcaa	taataaaaact	gaagtaccag	ttaaatatcc	480
aaaataatta	aaggaacatt	tttagcctgg	gtataattag	ctaattcact	ttacaagcat	540
ttattnagaa	tgaattcaca	tgttattatt	centagccca	acacaatgg		589

<210> 205

<211> 545

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(545)

<223> n = A,T,C or G

<400> 205

ttttttnttt	tttttttcagt	aataatcaga	acaatattta	tttttatatt	taaaattcat	60
agaaaagtgc	cttacattta	ataaaagtgt	gtttctcaaa	gtgatcagag	gaattagata	120
tngtcttgaa	caccaatatt	aatttgagga	aaatacacca	aaatacatta	agtaaatatt	180
ttaagatcat	agagcttgta	agtgaaaaga	taaaatttga	cctcagaaac	tctgagcatt	240
aaaaatccac	tattagcaaa	taaattacta	tggaacttct	gctttaattt	tgtgatgaat	300
atgggggtgc	actggtaaac	caacacattc	tgaaggatac	attacttagt	gatagattct	360
tatgtacttt	gctatanac	gtggatatga	gttgacaagt	ttctctttct	tcaatctttt	420
aaggggcnag	ngaaatgagg	aagaaaagaa	aaggattacg	catactgttc	tttctatngg	480
aaggattaga	tatgttttct	ttgccaatat	taaaaaaata	ataatgttta	ctactagtga	540
aaccc						545

<210> 206

<211> 487

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(487)

<223> n = A,T,C or G

<400> 206

tttttttttt ttttttagtc aagtttctna tttttattat aattaaagtc ttggtcattt	60
catttattag ctctgcaact tacatattta aattaaagaa acgttnttag acaactgtna	120
caatttataa atgtaagggt ccattattga gtanatatat tcctccaaga gtggatgtgt	180
cccttctccc accaactaat gaancagcaa cattagtta attttattag tagatnatac	240
actgctgcaa acgctaattc tcttctccat ccccatgtng atattgtgta tatgtgtgag	300
ttggttagaa tgcatacanca atctnacaat caacagcaag atgaagctag gcntgggctt	360
tcggtgaaaa tagactgtgt ctgtctgaat caaatgatct gacctatcct cgggtggcaag	420
aactcttcga accgcttcct caaaggcngc tgccacattt gtggcntctn ttgcacttgt	480
ttcaaaa	487

<210> 207

<211> 332

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(332)

<223> n = A,T,C or G

<400> 207

tgaattggt aaaagactgc atttttanaa ctagcaactc ttatttcttt cctttaaaaa	60
tacatagcat taaatcccaa atcctattta aagacctgac agcttgagaa ggtcactact	120
gcattttatag gaccttctgg tggttctgct gttacntttg aantctgaca atccttgana	180
atctttgcat gcagaggagg taaaaggat tggattttca cagaggaana acacagcgca	240
gaaatgaagg ggccaggctt actgagcttg tccactggag ggctcatggg tgggacatgg	300
aaaagaaggc agcctaggcc ctggggagcc ca	332

<210> 208

<211> 524

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(524)

<223> n = A,T,C or G

<400> 208

agggcgtggt ggggagggcg ttactgtttt gtctcagtaa caataaatc aaaaagactg	60
gttgtgttcc ggccccatcc aaccacgaag ttgatttctc ttgtgtgcag agtgactgat	120
tttaaaggac atggagcttg tcacaatgtc acaatgtcac agtggtgaagg gcacactcac	180
tcccgcgtga ttcacattta gcaaccaaca atagctcatg agtcatact tgtaaatact	240
tttggcagaa tacttnttga aacttgacaga tgataactaa gatccaagat atttcccaaa	300
gtaaatagaa gtgggtcata atattaatta cctgttcaca tcagcttcca tttacaagtc	360
atgagcccag acactgacat caaactaagc ccacttagac tcctcaccac cagtctgtcc	420
tgtcatcaga caggaggtg tcacttgac caaattctca ccagtcaatc atctatccaa	480
aaaccattac ctgatccact tccggtaatg caccaccttg gtga	524

<210> 209
 <211> 159
 <212> DNA
 <213> Homo sapien

<400> 209
 ggggtgaggaa atccagagtt gccatggaga aaattccagt gtcagcattc ttgctccttg 60
 tggccctctc ctacactctg gccagagata ccacagtcaa acctggagcc aaaaaggaca 120
 caaaggactc tcgacccaaa ctgccccaga ccctctcca 159

<210> 210
 <211> 256
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(256)
 <223> n = A,T,C or G

<400> 210
 actccctggc agacaaaggc agaggagaga gctctgttag ttctgtgttg ttgaactgcc 60
 actgaatttc ttccacttg gactattaca tgccanttga gggactaatg gaaaaacgta 120
 tggggagatt ttanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat 180
 ttgcaggggtg naaatgggan ggctggtttg ttanatgaac agggacatag gaggtaggca 240
 ccaggatgct aatca 256

<210> 211
 <211> 264
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(264)
 <223> n = A,T,C or G

<400> 211
 acattgtttt tttagataa agcattgaga gagctctcct taacgtgaca caatggaagg 60
 actggaacac ataccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt 120
 atattcaagc acatatgtta tatattatc agttccatgt ttatagccta gttaaggaga 180
 ggggagatac attcngaaag aggactgaaa gaaatactca agtnggaaaa cagaaaaaga 240
 aaaaaaggag caaatgagaa gcct 264

<210> 212
 <211> 328
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(328)
 <223> n = A,T,C or G

<400> 212
 acccaaaaat ccaatgctga atatttggtc tcattattcc canattcttt gattgtcaaa 60
 ggatttaatg ttgtctcagc ttgggcactt cagttaggac ctaaggatgc cagccggcag 120
 gtttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgccccccag 180

ttnaatttca ttccattga cttgggatcc ttatcatcag ccagagagat tgaaaattta 240
 cccctacnac tctttactct ctgganaggg ccagtgggtg tagctataag cttggccaca 300
 ttttttttct cttttactct ttgtcaga 328

<210> 213

<211> 250

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (250)

<223> n = A,T,C or G

<400> 213

acttatgagc agagcgacat atccnagtgt agactgaata aaactgaatt ctctccagtt 60
 taaagcattg ctactgaag ggatagaagt gactgccagg agggaaaagta agccaaggct 120
 cattatgcca aagganatat acattttcaat tctccaaact tcttcctcat tccaagagtt 180
 ttcaatattt gcatgaacct gctgataanc catgttaana aacaaatata tctctnacct 240
 tctcatcggt 250

<210> 214

<211> 444

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (444)

<223> n = A,T,C or G

<400> 214

accagaatc caatgctgaa tatttggtt cattattccc agattctttg attgtcaaag 60
 gatttaagt tgtctcagct tgggcacttc agttaggacc taaggatgcc agccggcagg 120
 tttatatag cagcaacaat attcaagcgc gacaacaggt tattgaactt gcccgccagt 180
 tgaatttcat tcccattgac ttgggatcct tatcatcagc canagagatt gaaaatttac 240
 cctacgact ctttactctc tggagagggc cagtgggtgt agctataagc ttggccacat 300
 ttttttttcc tttattcctt tgtcagagat gcgattcatc catatgctan aaaccaacag 360
 agtgactttt acaaaattcc tataganatt gtgaataaaa ccttacctat agttgccatt 420
 actttgctct cctaatata cctc 444

<210> 215

<211> 366

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (366)

<223> n = A,T,C or G

<400> 215

acttatgagc agagcgacat atccaagtgt anactgaata aaactgaatt ctctccagtt 60
 taaagcattg ctactgaag ggatagaagt gactgccagg agggaaaagta agccaaggct 120
 cattatgcca aagganatat acattttcaat tctccaaact tcttcctcat tccaagagtt 180
 ttcaatattt gcatgaacct gctgataagc catgttgaga aacaaatata tctctgacct 240
 tctcatcggt aagcagaggc ttaggcaac atggaccata gcgaanaaaa aacttagtaa 300
 tccaagctgt tttctacact gtaaccagggt ttccaaccaa ggtggaaatc tcctataact 360

ggtgcc

366

<210> 216

<211> 260

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(260)

<223> n = A,T,C or G

<400> 216

ctgtataaac agaactccac tgcangaggg agggccgggc caggagaatc tccgcttgtc	60
caagacaggg gcctaaggag ggtctccaca ctgctnntaa gggctnttnc atttttttat	120
taataaaaag tnnaaaaggc ctcttctcaa cttttttccc ttnggctgga aaatttaaaa	180
atcaaaaatt tcctnaagtt ntcaagctat catatatact ntatcctgaa aaagcaacat	240
aattcttctt tccctccttt	260

<210> 217

<211> 262

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(262)

<223> n = A,T,C or G

<400> 217

acctacgtgg gtaagtttan aaatgttata atttcaggaa naggaacgca tataattgta	60
tcttgcttat aattttctat tttaataagg aaatagcaaa ttgggggtggg gggaatgtag	120
ggcattctac agtttgagca aaatgcaatt aaatgtggaa ggacagcact gaaaaatttt	180
atgaataatc tgtatgatta tatgtctcta gagtagattt ataattagcc acttacccta	240
atataccttca tgcttgtaaa gt	262

<210> 218

<211> 205

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(205)

<223> n = A,T,C or G

<400> 218

accaaggtgg tgcattaccg gaantggatc aangacacca tcgtggccaa cccctgagca	60
cccctatcaa ctcccttttg tagtaaaactt ggaaccttgg aaatgaccag gccaaagactc	120
aggcctcccc agttctactg acctttgtcc ttangtntna ngtcagggt tgctaggaaa	180
anaaatcagc agacacaggt gtaaa	205

<210> 219

<211> 114

<212> DNA

<213> Homo sapien

<400> 219

tactgttttg tctcagtaac aataaatata aaaagactgg ttgtgttccg gcccacatcca 60
accacgaagt tgatttctct tgtgtgcaga gtgactgatt ttaaaggaca tgga 114

<210> 220

<211> 93

<212> DNA

<213> Homo sapien

<400> 220

actagccagc acaaaaaggca gggtagcctg aattgctttc tgctctttac atttctttta 60
aaataagcat ttagtgctca gtccctactg agt 93

<210> 221

<211> 167

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(167)

<223> n = A,T,C or G

<400> 221

actangtgca ggtgcgcaca aatatttgtc gatattccct tcactcttga ttccatgagg 60
tcttttgccc agcctgtggc tctactgtag taagtttctg ctgatgagga gccagnatgc 120
ccccactac cttccctgac gctccccana aatcacccaa cctctgt 167

<210> 222

<211> 351

<212> DNA

<213> Homo sapien

<400> 222

agggcgtggg gcggaggcg gtactgacct cattagtagg aggatgcatt ctggcacccc 60
gttcttcacc tgtcccccaa tccttaaaag gccatactgc ataaagtcaa caacagataa 120
atgtttgctg aattaaagga tggatgaaaa aaattaataa tgaatttttg cataatccaa 180
ttttctcttt tatatttcta gaagaagttt ctttgagcct attagatccc gggaatcttt 240
taggtgagca tgattagaga gcttgtaggt tgcttttaca tatacttggc atatttgagt 300
ctcgtatcaa aacaatagat tggtaaaggt ggtattattg tattgataag t 351

<210> 223

<211> 383

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(383)

<223> n = A,T,C or G

<400> 223

aaaacaaaca aacaaaaaaa acaattcttc attcagaaaa attatcttag ggactgatat 60
tggttaattat ggtcaattta atwrtrttkt ggggcatttc cttacattgt cttgacaaga 120
ttaaagtgc tgtgccaaaa tttgtattt tatttggaga cttcttatca aaagtaatgc 180
tgccaaagga agtctaagga attagtagtg tcccmcac ttgtttggag tgtgctattc 240
taaaagattt tgatttctg gaatgacaat tatattttaa ctttgggtggg ggaaanagtt 300
ataggaccac agtcttcact tctgatactt gtaaattaat cttttattgc acttgttttg 360
accattaagc tatatgttta aaa 383

<210> 224
 <211> 320
 <212> DNA
 <213> Homo sapien

<400> 224
 cccctgaagg cttcttgtta gaaaatagta cagttacaac caataggaac aacaaaaaga 60
 aaaagtttgt gacattgtag tagggagtgt gtacccctta ctccccatca aaaaaaaaaat 120
 ggatacatgg ttaaaggata raagggaat attttatcat atgttctaaa agagaaggaa 180
 gagaaaatac tactttctcr aaatggaagc ccttaaagggt gctttgatac tgaaggacac 240
 aaatgtggcc gtccatcctc ctttaragtt gcatgacttg gacacggtaa ctgttgacgt 300
 tttaractcm gcattgtgac 320

<210> 225
 <211> 1214
 <212> DNA
 <213> Homo sapien

<400> 225
 gaggactgca gcccgactc gcagccctgg caggcggcac tggtcattgga aaacgaattg 60
 ttctgctcgg gcgtcctggg gcatecgcag tgggtgctgt cagccgcaca ctgtttccag 120
 aactcctaca ccategggct gggcctgcac agtcttgagg ccgaccaaga gccagggagc 180
 cagatgggtgg aggccagcct ctccgtacgg caccagagt acaacagacc cttgctcgct 240
 aacgacctca tgctcatcaa gttggacgaa tccgtgtccg agtctgacac catccggagc 300
 atcagcattg cttcgcagtg ccctaccgcg gggaaactct gcctcgtttc tggctggggg 360
 ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg tgaacgtgtc ggtgggtgtc 420
 gaggaggtct gcagtaagct ctatgaccg ctgtaccacc ccagcatgtt ctgcgcgggc 480
 ggagggcaag accagaagga ctcttgaac ggtgactctg gggggcccct gatctgcaac 540
 gggtaacttg agggccttgt gtctttcgga aaagcccgt gtggccaagt tggcgtgcca 600
 ggtgtctaca ccaacctctg caaattcact gagtggatag agaaaaccgt ccaggccagt 660
 taactctggg gactgggaac ccatgaaatt gacccccaaa tacatcctgc ggaaggaatt 720
 caggaatc tgttcccagc ccctcctccc tcaggcccag gagtccaggc cccagcccc 780
 tcctccctca aaccaagggt acagatcccc agcccctcct ccctcagacc caggagtcca 840
 gacccccag cccctcctcc ctccagacca ggagtccagc ccctcctccc tcagaccag 900
 gagtccagac ccccagccc ctctcctc agaccagggt gtccaggccc ccaaccctc 960
 ctccctcaga ctccaggtc caagcccca accctcctt cccagacct agaggtccag 1020
 gtcccagccc ctctcctc agaccagcg gtccaatgcc acctagactc tccctgtaca 1080
 cagtgtcccc ttgtggcacg ttgacccaac cttaccagtt ggtttttcat tttttgtccc 1140
 tttccctag atccagaaat aaagtctaag agaagcgcaa aaaaaaaaaa aaaaaaaaaa 1200
 aaaaaaaaaa aaaa 1214

<210> 226
 <211> 119
 <212> DNA
 <213> Homo sapien

<400> 226
 acccagtatg tgcagggaga cggaacccca tgtgacagcc cactccacca gggttcccaa 60
 agaacctggc ccagtcataa tcattcatcc tgacagtggc aataatcacg ataaccagt 119

<210> 227
 <211> 818
 <212> DNA
 <213> Homo sapien

<400> 227
 acaattcata gggacgacca atgaggacag ggaatgaacc cggctctccc ccagccctga 60

tttttgctac	atatggggtc	ccttttcatt	ctttgcaaaa	acactggggtt	ttctgagaac	120
acggacgggt	cttagcacia	tttgtgaaat	ctgtgtaraa	cggggctttg	caggggagat	180
aattttcctc	ctctggagga	aaggtgggtga	ttgacaggca	gggagacagt	gacaaggcta	240
gagaaagcca	cgctcggcct	tctctgaacc	aggatggaac	ggcagacccc	tgaaaacgaa	300
gcttgteccc	ttccaatcag	ccactttctga	gaacccccat	ctaacttctc	actggaaaag	360
agggcctcct	caggagcagt	ccaagagttt	tcaaagataa	cgtgacaact	accatctaga	420
ggaaaagggtg	caccctcagc	agagaagccg	agagcttaac	tctggtcggt	tccagagaca	480
acctgctggc	tgtcttggga	tgcgcccagc	ctttgagagg	ccactacccc	atgaacttct	540
gccatccact	ggacatgaag	ctgaggacac	tgggcttcaa	cactgagttg	tcatgagagg	600
gacaggctct	gccctcaagc	cggctgaggg	cagcaaccac	tctcctcccc	tttctcacgc	660
aaagccattc	ccacaaatcc	agaccatacc	atgaagcaac	gagacccaaa	cagtttggtc	720
caagaggata	tgaggactgt	ctcagcctgg	ctttgggctg	acaccatgca	cacacacaag	780
gtccacttct	aggttttcag	cctagatggg	agtcgtgt			818

<210> 228

<211> 744

<212> DNA

<213> Homo sapien

<400> 228

actggagaca	ctgttgaact	tgatcaagac	ccagaccacc	ccaggctctcc	ttcgtgggat	60
gtcatgacgt	ttgacatacc	tttggaaacga	gcctcctcct	tggaagatgg	aagaccgtgt	120
tcgtggccga	cctggcctct	cctggcctgt	ttcttaagat	gcggagtcac	atttcaatgg	180
taggaaaagt	ggcttcgtaa	aatagaagag	cagtcactgt	ggaactacca	aatggcgaga	240
tgctcgggtc	acattggggg	gctttgggat	aaaagattta	tgagccaact	attctctggc	300
accagattct	aggccagttt	gttccactga	agcttttccc	acagcagtc	acctctgcag	360
gctggcagct	gaatggcttg	ccgggtggctc	tgtggcaaga	tcacactgag	atcgatgggt	420
gagaaggcta	ggatgcttgt	ctagtgttct	tagctgtcac	gttggctcct	tccaggttgg	480
ccagacgggtg	ttggccactc	ccttctaaaa	cacaggcgcc	ctcctgggtga	cagtgaacctg	540
ccgtgggtatg	ccttggccca	ttccagcagt	cccagttatg	catttcaagt	ttgggggttg	600
ttcttttcgt	taatgttctc	ctgtgttgct	agctgtcttc	atttctctgg	ctaagcagca	660
ttgggagatg	tggaccagag	atccactcct	taagaaccag	tggcgaaaga	cactttcttt	720
cttactctctg	aagtagctgg	tggt				744

<210> 229

<211> 300

<212> DNA

<213> Homo sapien

<400> 229

cgagtctggg	ttttgtctat	aaagtttgat	ccctcctttt	ctcatccaaa	tcatgtgaac	60
cattacacat	cgaaataaaa	gaaaggtggc	agacttgccc	aacgccaggc	tgacatgtgc	120
tgagggttg	ttgtttttta	attattattg	ttagaaacgt	caccacagct	cctgtttaat	180
ttgtatgtga	cagccaaactc	tgagaaggtc	ctatttttcc	acctgcagag	gatccagtct	240
cactaaggctc	ctccttgccc	tcacactgga	gtctccgcca	gtgtgggtgc	ccactgacat	300

<210> 230

<211> 301

<212> DNA

<213> Homo sapien

<400> 230

cagcagaaca	aatacaata	tgaagagtgc	aaagatctca	taaaatctat	gctgaggaat	60
gagcgacagt	tcaaggagga	gaagcttgca	gagcagctca	agcaagctga	ggagctcagg	120
caatataaag	tctgtgttca	cactcaggaa	cgagagctga	cccagttaag	ggagaagttg	180
cgggaaggga	gagatgcctc	cctctcattg	aatgagcate	tccaggccct	cctcactccg	240
gatgaaccgg	acaagtccca	ggggcaggac	ctccaagaaa	cagacctcgg	ccgcgaccac	300
g						301

<210> 231
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 231
 gcaagcacgc tggcaaatct ctgtcaggtc agctccagag aagccattag tcatttttagc 60
 caggaactcc aagtccacat ccttggcaac tggggacttg cgcagggttag ccttgaggat 120
 ggcaacacgg gactttctcat caggaagtgg gatgtagatg agctgatcaa gacggccagg 180
 tctgaggatg gcaggatcaa tgatgtcagg ccggttggtta ccgccaatga tgaacacatt 240
 tttttttgtg gacatgccat ccattttctgt caggatctgg ttgatgactc ggtcagcagc 300
 c 301

<210> 232
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 232
 agtaggtatt tcgtgagaag ttcaacacca aaactggaac atagttcttc ttcaagtgtt 60
 ggcgacagcg gggcttcctg attctggaat ataactttgt gttaaattaac agccacctat 120
 agaagagtcc atctgctgtg aaggagagac agagaactct gggttccgtc gtctgttcca 180
 cgtgctgtac caagtgtctg tgccagcctg ttacctgttc tcaactgaaa tctggctaata 240
 gctcttgtgt atcacttctg attctgacaa tcaatcaatc aatggcctag agcactgact 300
 g 301

<210> 233
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 233
 atgactgact tcccagtaag gctctctaa gggtaagtag gaggatccac aggatttgag 60
 atgctaaggc cccagagatc gtttgatcca accctcttat tttcagaggg gaaaatgggg 120
 cctagaagtt acagagcatc tagctggtgc gctggcacc cttggcctcac acagactccc 180
 gagtagctgg gactacaggc acacagtcac tgaagcaggc cctgttagca attctatgcg 240
 taaaaattaa catgagatga gtagagactt tattgagaaa gcaagagaaa atcctatcaa 300
 c 301

<210> 234
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 234
 aggtcctaca catcgagact catccatgat tgatatgaat ttaaaaatta caagcaaaga 60
 cattttatcc atcatgatgc tttcttttgt ttcttctttt cgttttcttc tttttctttt 120
 tcaatttcag caacatactt ctcaatttct tcaggattta aaatcttgag ggattgatct 180
 cgctcatga cagcaagttc aatgtttttg ccacctgact gaaccacttc caggagtgcc 240
 ttgatcacca gcttaatggg cagatcatct gttcaatgg cttcgtcagt atagttcttc 300
 t 301

<210> 235
 <211> 283
 <212> DNA
 <213> Homo sapien

<400> 235

tggggctgtg catcaggcgg gtttgagaaa tattcaattc tcagcagaag ccagaatttg	60
aattccctca tcttttaggg aatcatttac caggtttggg gaggattcag acagctcagg	120
tgctttcact aatgtctctg aacttctgtc cctctttgtt catggatagt ccaataaata	180
atgttatctt tgaactgatg ctcataggag agaataaag aactctgagt gatatcaaca	240
ttagggattc aaagaaatat tagatttaag ctcacactgg tca	283

<210> 236

<211> 301

<212> DNA

<213> Homo sapien

<400> 236

aggtcctcca ccaactgcct gaagcacggg taaaattggg aagaagtata gtgcagcata	60
aatactttta aatcgatcag atttccctaa cccacatgca atcttcttca ccagaagagg	120
tcggagcagc atcatthaata ccaagcagaa tgcgtaatag ataaatacaa tggatatatag	180
tgggtagacg gcttcatgag tacagtgtac tgtggatcgc taatctggac ttgggttgta	240
aagcatcgtg taccagtcag aaagcatcaa tactcgacat gaacgaatat aaagaacacc	300
a	301

<210> 237

<211> 301

<212> DNA

<213> Homo sapien

<400> 237

cagtggtagt ggtgggtggac gtggcggttg tctgtgtgcc ttttttggtg cccgtcacaa	60
actcaatttt tgttcgctcc tttttggcct tttccaattt gtccatctca attttctggg	120
ccttggctaa tgcctcatag taggagtcct cagaccagcc atggggatca aacatatcct	180
ttgggtagtt ggtgccaaagc tctgcaatgg cacagaatgg atcagcttct cgtaaatcta	240
gggttccgaa attcttttct cctttggata atgtagttca tatccattcc ctcctttate	300
t	301

<210> 238

<211> 301

<212> DNA

<213> Homo sapien

<400> 238

gggcaggttt tttttttttt ttttttgatg gtgcagaccc ttgctttatt tgtctgactt	60
gttcacagtt cagccccctg ctcagaaaac caacgggcca gctaaggaga ggaggaggca	120
ccttgagact tccggagtcg aggtctctca gggttcccca gcccatcaat cattttctgc	180
acccccgcc tgggaagcag ctccctgggg ggtgggaatg ggtgactaga agggatttca	240
gtgtgggacc caggggtctgt tcttcacagt agggaggtgga agggatgact aatttcttta	300
t	301

<210> 239

<211> 239

<212> DNA

<213> Homo sapien

<400> 239

ataagcagct agggaattct ttatttagta atgtcctaac ataaaagtgc acataactgc	60
ttctgtcaaa ccatgatact gagctttgtg acaaccaga aataactaag agaaggcaaa	120
cataatacct tagagatcaa gaaacattta cacagttcaa ctgttttaaa atagctcaac	180
attcagccag tgagtagagt gtgaatgcca gcatacacag tatacaggtc cttcaggga	239

<210> 240

<211> 300
 <212> DNA
 <213> Homo sapien

<400> 240
 gggtcctaag aagcagcagc ttccacattt taacgcaggt ttacgggtgat actgtccttt 60
 gggatctgcc ctccagtggg acctttttaag gaagaagtgg gcccaagcta agttccacat 120
 gctgggtgag ccagatgact tctgttccct gggtcactttc ttcaatgggg cgaatggggg 180
 ctgccaggtt tttaaaatca tgcttcatct tgaagcacac gggtcacttca ccctcctcac 240
 gctgtgggtg tactttgatg aaaataccca ctttgttggc ctttctgaag ctataatgtc 300

<210> 241
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 241
 gaggtctggt gctgaggtct ctgggctagg aagaggagtt ctgtggagct ggaagccaga 60
 cctcttttga ggaaactcca gcagctatgt tgggtgtctct gaggggaatgc aacaaggctg 120
 ctctccatg tattggaaaa ctgcaaaactg gactcaactg gaaggaagtg ctgctgccag 180
 tgtgaagaac cagcctgagg tgacagaaac ggaagcaaac aggaacagcc agtcttttct 240
 tcctcctcct gtcatacggc ctctctcaag catcctttgt tgtcaggggc ctaaaaggga 300
 g 301

<210> 242
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 242
 ccgaggtcct gggatgcaac caatcactct gtttcacgtg acttttatca ccatacaatt 60
 tgtggcattt cctcattttc tacattgtag aatcaagagt gtaaataaat gtatatcgat 120
 gtcttcaaga atatatcatt cctttttcac tagaaccat tcaaaatata agtcaagaat 180
 cttaatatca acaaataat caagcaaact ggaaggcaga ataactacca taatttagta 240
 taagtaccca aagttttata aatcaaaagc cctaatagata accattttta gaattcaatc 300
 a 301

<210> 243
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 243
 aggtaagtcc cagtttgaag ctcaaaagat ctggtatgag cataggctca tcgacgacat 60
 ggtggcccaa gctatgaaat cagagggagg cttcatctgg gcctgtaaaa actatgatgg 120
 tgacgtgcag tcggactctg tggcccaagg gtatggctct ctggcatga tgaccagcgt 180
 gctggtttgt ccagatggca agacagtaga agcagaggct gccacggga ctgtaaccgc 240
 tctactaccgc atgttccaga aaggacagga gacgtccacc aatcccattg cttccatttt 300
 t 301

<210> 244
 <211> 300
 <212> DNA
 <213> Homo sapien

<400> 244
 gctggtttgc aagaatgaaa tgaatgatcc tacagctagg acttaacctt gaaatggaaa 60
 gtcatgcaat cccatttgca ggatctgtct gtgcacatgc ctctgtagag agcagcattc 120

ccagggacct tggaaacagt tgacactgta aggtgcttgc tccccaagac acatcctaaa 180
aggtgttgta atggtgaaaa cgtcttcctt ctttattgcc cttctctatt tatgtgaaca 240
actgtttgtc ttttgtgtat cttttttaaa ctgtaaagtt caattgtgaa aatgaatatt 300

<210> 245

<211> 301

<212> DNA

<213> Homo sapien

<400> 245

gtctgagtat ttaaaatggt attgaaatta tccccaacca atgttagaaa agaagaggt 60
tatatactta gataaaaaat gaggtgaatt actatccatt gaaatcatgc tcttagaatt 120
aagggcagga gatattgtca ttaatgtara cttcaggaca ctagagtata gcagccctat 180
gttttcaaag agcagagatg caattaaata ttgttttagca tcaaaaaggc cactcaatac 240
agctaataaa atgaaagacc taatttctaa agcaattctt tataattttac aaagttttta 300
g 301

<210> 246

<211> 301

<212> DNA

<213> Homo sapien

<400> 246

ggtctgtcct acaatgcctg cttcttgaaa gaagtcggca ctttctagaa tagctaaata 60
acctgggctt attttaaaga actatttgta gctcagattg gttttcctat ggctaaaata 120
agtgtcttct gtgaaaatta aataaaacag ttaattcaaa gccttgatat atgttaccac 180
taacaatcat actaaatata ttttgaagta caaagtttga catgctctaa agtgacaacc 240
caaagtgtgc ttacaaaaca cgttcctaac aaggtatgct ttacactacc aatgcagaaa 300
c 301

<210> 247

<211> 301

<212> DNA

<213> Homo sapien

<400> 247

aggtcctttg gcagggctca tggatcagag ctcaaactgg agggaaaggc atttcgggta 60
gcctaagagg gcgactggcg gcagcacaac caaggaaggc aaggttggtt cccccacgct 120
gtgtcctgtg ttcaggtgcg acacacaatc ctcatgggaa caggatcacc catgcgctgc 180
ccttgatgat caaggttggg gcttaagtgg attaagggag gcaagttctg gggtccttgc 240
cttttcaaac catgaagtca ggctctgtat ccctcctttt cctaactgat attctaacta 300
a 301

<210> 248

<211> 301

<212> DNA

<213> Homo sapien

<400> 248

aggtccttgg agatgccatt tcagccgaag gactcttctw ttcggaagta caccctcact 60
attaggaaga ttcttagggg taatttttct gaggaaggag aactagccaa cttagaatt 120
acaggaagaa agtggttttg aagacagcca aagaaataaa agcagattaa attgtatcag 180
gtacattcca gcctgtttgg aactccataa aaacatttca gatttttaac ccgaatttag 240
ctaattgagac tggatttttg ttttttatgt tgtgtgtcgc agagctaaaa actcagttcc 300
c 301

<210> 249

<211> 301

<212> DNA

<213> Homo sapien

<400> 249

gtccagagga agcacctggg gctgaactag gcttgccctg ctgtgaactt gcacttggag	60
ccctgacgct gctgttctcc ccgaaaaacc cgaccgacct ccgcgatctc cgccccgcc	120
ccagggagac acagcagtga ctcagagctg gtcgcacact gtgcctccct cctcaccgcc	180
catcgtaatg aattatcttg aaaattaatt ccaccatcct ttcagattct ggatggaaag	240
actgaatctt tgactcagaa ttgtttgctg aaaagaatga tgtgactttc ttagtcattt	300
a	301

<210> 250

<211> 301

<212> DNA

<213> Homo sapien

<400> 250

ggtctgtgac aaggacttgc aggctgtggg aggcaagtga cccttaacac tacacttctc	60
cttatcttta ttggcttgat aaacataatt atttctaaca ctagcttatt tccagttgcc	120
cataagcaca tcagtacttt tctctggctg gaatagtaaa ctaaagtatg gtacatctac	180
ctaaaagact actatgtgga ataatacata ctaatgaagt attacatgat ttaaagacta	240
caataaaacc aaacatgctt ataacattaa gaaaaacaat aaagatacat gattgaaacc	300
a	301

<210> 251

<211> 301

<212> DNA

<213> Homo sapien

<400> 251

gccgaggtcc tacatttggc ccagtttccc cctgcatect ctccagggcc cctgcctcat	60
agacaacctc atagagcata ggagaactgg ttgccctggg ggcaggggga ctgtctggat	120
ggcaggggtc ctcaaaaatg ccactgtcac tgccaggaaa tgcttctgag cagtacacct	180
cattgggatc aatgaaaagc ttcaagaaat ctccaggctc actctcttga aggccccgaa	240
cctctggagg ggggcagtgg aatcccagct ccaggacgga tcctgtcgaa aagatatact	300
c	301

<210> 252

<211> 301

<212> DNA

<213> Homo sapien

<400> 252

gcaaccaatc actctgtttc acgtgacttt taccaccata caatttgttg catttcctca	60
ttttctacat tgtagaatca agagtgtaaa taaatgtata tcgatgtctt caagaatata	120
tcattccttt ttacttagga acccattcaa aatataagtc aagaatctta atatcaacaa	180
atatatcaag caaactggaa ggcagaataa ctaccataat ttagtataag taccctaaag	240
tttataaatc aaaagcccta atgataacca tttttagaat tcaatcatca ctgtagaatc	300
a	301

<210> 253

<211> 301

<212> DNA

<213> Homo sapien

<400> 253

ttccctaaga agatgttatt ttgttgggtt ttgttcccc tccatctcga ttctcgtacc	60
caactaaaaa aaaaaataa agaaaaaatg tgctgcgttc tgaaaaataa ctcttagct	120

```

tggctctgatt gttttcagac cttaaaatat aaacttgttt cacaagcttt aatccatgtg      180
gattttttttt cttagagaac cacaaaacat aaaaggagca agtcggactg aatacctgtt      240
tccatagtgc ccacagggtta ttcctcacat tttctccata ggaaaatgct ttttcccaag      300
g                                                                                   301

```

```

<210> 254
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 254
cgctgcgcct ttcccttggg ggaggggcaa ggccagaggg ggtccaagtg cagcacgagg      60
aacttgacca attcccttga agcgggtggg ttaaaccctg taaatgggaa caaaatcccc      120
ccaaatctct tcatcttacc ctggtggact cctgactgta gaattttttg gttgaaacaa      180
gaaaaaata aagcttttga cttttcaagg ttgcttaaca ggtactgaaa gactggcctc      240
acttaactg agccaggaaa agctgcagat ttattaatgg gtgtgttagt gtgcagtgcc      300
t                                                                                   301

```

```

<210> 255
<211> 302
<212> DNA
<213> Homo sapien

```

```

<400> 255
agctttttttt tttttttttt tttttttttt ttcattaaaa aatagtgtct tttattataa      60
attactgaaa tgtttctttt ctgaatataa atataaatat gtgcaaagtt tgacttggat      120
tggtgattttg ttgagttctt caagcatctc ctaataccct caagggcctg agtagggggg      180
aggaaaaagg actggagggtg gaatctttat aaaaaacaag agtgattgag gcagattgta      240
aacattatta aaaaacaaga aacaaacaaa aaaatagaga aaaaaaccac cccaacacac      300
aa                                                                                   302

```

```

<210> 256
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 256
gttccagaaa acattgaagg tggcttccca aagtctaact agggataccc cctctagcct      60
aggacccttc tccccacacc tcaatccacc aaaccatcca taatgcaccc agataggccc      120
acccccaaaa gcctggacac cttgagcaca cagttatgac caggacagac tcatctctat      180
aggcaaatag ctgctggcaa actggcatta cctggtttgt ggggatgggg gggcaagtgt      240
gtggcctctc ggcctgggta gcaagaacat tcagggtagg cctaaagtta tcgtgttagt      300
t                                                                                   301

```

```

<210> 257
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 257
gttgtggagg aactctggct tgctcattaa gtccactga ttttactat cccctgaatt      60
tccccactta tttttgtctt tcaactatgc aggccttaga agaggtctac ctgcctccag      120
tcttacctag tccagtctac cccctggagt tagaatggcc atcctgaagt gaaaagtaat      180

```

```

gtcacattac tcccttcagt gattttcttgt agaagtgcc atccctgaat gccaccaaga      240
tcttaatctt cacatcttta atcttatctc tttgactcct ctttacaccg gagaaggctc      300
c                                                                           301

```

```

<210> 258
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 258
cagcagtagt agatgccgta tgccagcacg cccagcactc ccaggatcag caccagcacc      60
aggggcccag ccaccaggcg cagaagcaag ataaacagta ggctcaagac cagagccacc      120
cccagggcaa caagaatcca ataccaggac tgggcaaaat cttcaaagat cttaacactg      180
atgtctcggg cattgaggct gtcaataana cgctgatccc ctgctgtatg gtggtgtcat      240
tggtgatccc tgggagcgcc ggtggagtaa cgttggtcca tggaaagcag cgcccacaac      300
t                                                                           301

```

```

<210> 259
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 259
tcatatatgc aaacaaatgc agactangcc tcaggcagag actaaaggac atctcttggg      60
gtgtcctgaa gtgatttggg cccctgaggg cagacaccta agtaggaatc ccagtgggaa      120
gcaaagccat aaggaaagccc aggattcctt gtgatcagga agtgggcccag gaaggctctg      180
tccagctcac atctcatctg catgcagcac ggaccggatg cgccactgg gtcttggctt      240
ccctcccac ttctcaagca gtgtccttgt tgagccattt gcataccttg ctccagggtg      300
c                                                                           301

```

```

<210> 260
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 260
ttttttttct ccctaaggaa aaagaaggaa caagtctcat aaaaccaa at aagcaatgg      60
aaggtgtctt aacttgaaaa agattaggag tcaactggtt acaagttata attgaatgaa      120
agaactgtaa cagccacagt tggccatttc atgccaatgg cagcaaaca caggattaac      180
tagggcaaaa taaataagtg tgtggaagcc ctgataagtg cttaataaac agactgattc      240
actgagacat cagtacctgc ccgggcggcc gctcgagccg aattctgcag atatccatca      300
c                                                                           301

```

```

<210> 261
<211> 301
<212> DNA
<213> Homo sapien

```

<400> 261

```

aatattcga gcaaactctg taactaatgt gtctccataa aaggctttga actcagtga 60
tctgcttcca tccacgattc tagcaatgac ctctcggaca tcaaagctcc tcttaagggt 120
agcaccaact attccataca attcatcagc aggaaataaa ggctcttcag aagggtcaat 180
ggtgacatcc aatttcttct gataatttag attcctcaca accttcttag ttaagtgaag 240
ggcatgatga tcattccaaag cccagtgggc acttactcca gactttctgc aatgaagatc 300
a 301

```

<210> 262

<211> 301

<212> DNA

<213> Homo sapien

<400> 262

```

gaggagagcc tgttacagca tttgtaagca cagaatactc caggagtatt tgtaattgtc 60
tgtgagcttc ttgccgcaag tctctcagaa atttaaaaag atgcaaattcc ctgagtcacc 120
cctagacttc ctaaaccaga tcctctgggg ctggaacctg gcaactctgca ttgtaatga 180
gggctttctg gtgcacacct aattttgtgc atctttgccc taaatcctgg attagtgtcc 240
catcattacc cccacattat aatgggatag attcagagca gatactctcc agcaaagaat 300
c 301

```

<210> 263

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 263

```

tttagcttgt ggtaaatgac tcacaaaact gattttaaaa tcaagttaat gtgaattttg 60
aaaattacta cttaatccta attcacaata acaatggcat taagggttga cttgagttgg 120
ttcttagtat tatttatggg aaataggctc ttaccacttg caaataactg gccacatcat 180
taatgactga cttcccagta aggctctcta aggggtaagt angaggatcc acaggatttg 240
agatgctaag gcccagaga tcgtttgatc caacctctt attttcagag gggaaaatgg 300
g 301

```

<210> 264

<211> 301

<212> DNA

<213> Homo sapien

<400> 264

```

aaagacgtta aaccactcta ctaccacttg tggaactctc aaagggtaaa tgacaaaacc 60
aatgaatgac tctaaaaaca atatttacat ttaatggttt gtagacaata aaaaaacaag 120
gtggatagat ctagaattgt aacattttta gaaaaccata scatttgaca gatgagaaaag 180
ctcaattata gatgcaaagt tataactaaa ctactatagt agtaaagaaa tacatttcac 240
acccttcata taaattcact atcttggctt gaggcactcc ataaaatgta tcacgtgcac 300
a 301

```

<210> 265

<211> 301

<212> DNA

<213> Homo sapien

<400> 265

tgcccaagtt atgtgtaagt gtatccgcac ccagaggtaa aactacactg tcatctttgt	60
cttcttgtga cgcagtattt cttctctggg gagaagccgg gaagtcttct cctggctcta	120
catattcttg gaagtctcta atcaactttt gtccatttg ttccatttct tcaggaggga	180
ttttcagttt gtcaacatgt tctctaaca cacttgccca tttctgtaaa gaatccaaag	240
cagtccaagg ctttgacatg tcaacaacca gcataactag agtatccttc agagatacgg	300
c	301

<210> 266

<211> 301

<212> DNA

<213> Homo sapien

<400> 266

taccgtctgc ccttctctcc atccaggcca tctgcgaatc tacatgggtc ctctattcgc	60
acaccagatc actcttttct ctaccacag gcttgctatg agcaagagac acaacctcct	120
ctcttctgtg ttccagcttc ttttctgtt ctteccaccc cttaagttct attcctgggg	180
atagagacac caatacccat aacctctctc ctaagcctcc ttataacca ggtgacacag	240
cacagactcc tgacaactgg taaggccaat gaactgggag ctcacagctg gctgtgctg	300
a	301

<210> 267

<211> 301

<212> DNA

<213> Homo sapien

<400> 267

aaagagcaca ggccagctca gcctgccctg gccatctaga ctcagcctgg ctccatgggg	60
gttctcagtg ctgagtcctat ccaggaaaag ctcacctaga cttctgagg ctgaatcttc	120
atcctcacag gcagcttctg agagcctgat attcctagcc ttgatgggtc ggagtaaagc	180
ctcattctga ttctctcct tcttttctt caagttggct ttctcacat ccctctgttc	240
aattcgcttc agcttgtctg ctttagccct catttccaga agcttcttct ctttggcatc	300
t	301

<210> 268

<211> 301

<212> DNA

<213> Homo sapien

<400> 268

aatgtctcac tcaactactt cccagcctac cgtggcctaa ttctgggagt tttcttctta	60
gatcttggga gagctgggtc ttctaaggag aaggaggaag gacagatgta actttggatc	120
tcgaagagga agtctaattg aagtaattag tcaacggtcc ttgttttagac tcttgggaata	180
tgctgggtgg ctcatgagc ctttttgag aaagcaagta ttattcttaa ggagtaacca	240
cttcccatg ttctacttct taccatcatc aattgtatat tatgtattct ttggagaact	300
a	301

<210> 269

<211> 301

<212> DNA

<213> Homo sapien

<400> 269

taacaatata cactagctat ctttttaact gtccatcatt agcaccaatg aagattcaat	60
aaaattacct ttattcacac atctcaaac aattctgcaa attcttagtg aagtttaact	120
atagtcacag acctaaata ttcacattgt tttctatgtc tactgaaaat aagttcacta	180
cttttctgga tattctttac aaaatcttat taaaattcct ggtattatca cccccaatta	240
tacagtagca caaccacctt atgtagtttt tacatgatag ctctgtagaa gtttcacatc	300
t	301

<210> 270
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 270
 cattgaagag cttttgcgaa acatcagaac acaagtgcctt ataaaattaa ttaagcctta 60
 cacaagaata catattcctt ttatttctaa ggagttaaac atagatgtag ctgatgtgga 120
 gagcttgctg gtgcagtgca tattggataa cactattcat ggccgaattg atcaagtcaa 180
 ccaactcctt gaactggatc atcagaagaa ggggtggtgca cgatatactg cactagataa 240
 tggaccaacc aactaaattc tctcaccagg ctgtatcagt aaactggcctt aacagaaaac 300
 a 301

<210> 271
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)... (301)
 <223> n = A,T,C or G

<400> 271
 aaaaggttct cataagatta acaattttaa taaatatttg atagaacatt ctttctcatt 60
 tttatagetc atcttttaggg ttgatattca gttcatgcct cccttgctgt tcttgatcca 120
 gaattgcaat cacttcatca gcttgatttc gctccaattc tctataaagt gggccaagg 180
 tgaaccacag agccacagca cacctctttc ccttggtgac tgccttcacc ccatganggt 240
 tctctctccc agatganaac tgatcatgcg cccacatttt_gggttttata gaagcagtca 300
 c 301

<210> 272
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 272
 taaattgcta agccacagat aacaccaatc aaatggaaca aatcactgtc ttcaaagtgc 60
 ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtatttagga 120
 tccaataatt cctcatgat gagcaagaaa aattctttgc gcacccctcc tgcattccaca 180
 gcatcttctc caacaaatat aaccttgagt ggcttcttgt aatctatgtt ctttgtttcc 240
 ctaaggactt ccattgcac tctacaata ttttctctac gcaccactag aattaagcag 300
 g 301

<210> 273
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)... (301)
 <223> n = A,T,C or G

<400> 273
 acatgtgtgt atgtgtatct ttgggaaaaa aanaagacat cttgtttayt atttttttgg 60
 agagangctg ggacatggat aatcacwtaa ttgtctayta tyactttaat ctgactygaa 120

```

gaaccgtcta aaaataaaat ttaccatgtc dtatatctct tatagtatgc ttatttcacc      180
ttytttctgt ccagagagag tatcagtgac ananatttma ggggtgaamac atgmattgggt      240
gggacttnty tttaengagm accctgcccc sgcgccctcg makcngantt ccgcsananc      300
t                                                                                   301

```

<210> 274

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 274

```

cttatatact ctttctcaga ggcaaaagag gagatgggta atgtagacaa ttctttgagg      60
aacagtaaatt gattattaga gagaangaat ggaccaagga gacagaaatt aacttgtaaa      120
tgattctctt tggaatctga atgagatcaa gaggccagct ttagcttggtg gaaaagtcca      180
tctaggtatg gttgcattct cgtcttcttt tctgcagtag ataatgaggt aaccgaaggc      240
aattgtgctt cttttgataa gaagctttct tggcatatc aggaaattcc aganaaaagtc      300
c                                                                                   301

```

<210> 275

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 275

```

tcggtgtcag cagcacgtgg cattgaacat tgcaatgtgg agcccaaacc acagaaaatg      60
gggtgaaatt ggccaacttt ctattaactt atgttggaac ttttgccacc aacagtaagc      120
tgcccttctt aataaaagaa aattgaaagg tttctcacta aacggaatta agtagtgag      180
tcaagagact cccaggcctc agcgtacctg cccgggcggc cgctcgaagc cgaattctgc      240
agatatccat cacactggcg gncgctcgan catgcatcta gaaggnccaa ttcgccctat      300
a                                                                                   301

```

<210> 276

<211> 301

<212> DNA

<213> Homo sapien

<400> 276

```

tgtacacata ctcaataaat aaatgactgc attgtggtat tattactata ctgattatat      60
ttatcatgtg acttctaatt agaaaatgta tccaaaagca aaacagcaga tatacaaaat      120
taaagagaca gaagatagac attaacagat aaggcaactt atacattgag aatccaaatc      180
caatacattt aaacatttgg gaaatgaggg ggacaaatgg aagccagatc aaatttgtgt      240
aaaactattc agtatgttcc cttgcttca tgtctgagaa ggctctcctt caatggggat      300
g                                                                                   301

```

<210> 277

<211> 301

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 277
 ttgttgatg tcagtatttt attacttgcg ttatgagtgc tcacctggga aattctaaag 60
 atacagagga cttggaggaa gcagagcaac tgaatttaat ttaaaagaag gaaaacattg 120
 gaatcatggc actcctgata ctttcccaaa tcaacactct caatgcccc aacctgctct 180
 caccatagtg gggagactaa agtggccacg gatttgcctt angtgtgcag tgcgttctga 240
 gttcnctgtc gattacatct gaccagtctc ctttttccga agtcntccg ttcaatcttg 300
 c 301

<210> 278
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 278
 taccactaca ctccagcctg ggcaacagag caagacctgt ctcaaagcat aaaatggaat 60
 aacatatcaa atgaaacagg gaaaatgaag ctgacaatatt atggaagcca gggcttgtca 120
 cagtctctac tgttattatg cattacctgg gaatttatat aagcccttaa taataatgcc 180
 aatgaacatc tcatgtgtgc tcacaatggt ctggcactat tataagtgtc tcacagggtt 240
 tatgtgttct tcgtaacttt atggantagg tactcggccg cgaacacgct aagccgaatt 300
 c 301

<210> 279
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 279
 aaagcaggaa tgacaaaagct tgcttttctg gtatgttcta ggtgtattgt gacttttact 60
 gttatattaa ttgccaatat aagtaaata agattatata tgtatagtgt ttcacaaagc 120
 ttagaccttt accttccagc caccacacag tgcttgatat ttcagagtca gtcattgggt 180
 atacatgtgt agttccaaag cacataagct agaanaanaa atatttctag ggagcactac 240
 catctgtttt cacatgaaat gccacacaca tagaactcca acatcaattt cattgcacag 300
 a 301

<210> 280
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 280
 ggtactggag ttttctccc ctgtgaaaac gtaactactg ttgggagtga attgaggatg 60
 tagaaaggtg gtggaaccaa attgtggtca atggaaatag gagaatatgg ttctcactct 120

tgagaaaaaa	acctaagatt	agcccaggta	gttgectgta	acttcagttt	ttctgectgg	180
gtttgatata	gtttagggtt	gggggttagat	taagatctaa	attacatcag	gacaaagaga	240
cagactatta	actccacagt	taattaagga	ggtatgttcc	atgtttattt	gttaaagcag	300
t						301

<210> 281

<211> 301

<212> DNA

<213> Homo sapien

<400> 281

aggtacaaga	aggggaatgg	gaaagagctg	ctgctgtggc	attgttcaac	ttggatattc	60
gccgagcaat	ccaaatcctg	aatgaagggg	catcttctga	aaaaggagat	ctgaatctca	120
atgtggtagc	aatggcctta	tcgggttata	cggatgagaa	gaactccctt	tggagagaaa	180
tgtgtagcac	actgcgatta	cagctaaata	acccgtattt	gtgtgtcatg	tttgcatttc	240
tgacaagtga	aacaggatct	tacgatggag	ttttgtatga	aaacaaagtt	gcagtacctc	300
g						301

<210> 282

<211> 301

<212> DNA

<213> Homo sapien

<400> 282

caggtactac	agaattaaaa	tactgacaag	caagtagttt	cttggcgtgc	acgaattgca	60
tccagaaccc	aaaaattaa	aaattcaaaa	agacattttg	tgggcacctg	ctagcacaga	120
agcgcagaag	caaagcccag	gcagaaccat	gtaacctta	cagctcagcc	tgcacagaag	180
cgcagaagca	aagcccaggc	agaaccatgc	taaccttaca	gtcagcctg	cacagaagcg	240
cagaagcaaa	gcccaggcag	aacatgctaa	ccttacagct	cagcctgcac	agaagcacag	300
a						301

<210> 283

<211> 301

<212> DNA

<213> Homo sapien

<400> 283

atctgtatac	ggcagacaaa	ctttatarag	tgtagagagg	tgagcgaaag	gatgcaaaag	60
cactttgagg	gctttataat	aatatgctgc	ttgaaaaaaa	aaatgtgtag	ttgatactca	120
gtgcatctcc	agacatagta	aggggttgct	ctgaccaatc	aggtgatcat	tttttctatc	180
acttcccagg	ttttatgcaa	aaattttggt	aaattctata	atggtgatat	gcattcttta	240
ggaaacatat	acatttttta	aaatctattt	tatgtaagaa	ctgacagacg	aatttgcttt	300
g						301

<210> 284

<211> 301

<212> DNA

<213> Homo sapien

<400> 284

caggtacaaa	acgctattaa	gtggcttaga	atttgaacat	ttgtggtctt	tatttacttt	60
gcttcgtgtg	tgggcaaaagc	aacatcttcc	ctaaatatat	attaccaaga	aaagcaagaa	120
gcagattagg	tttttgacaa	aacaaacagg	ccaaaagggg	gctgacctgg	agcagagcat	180
ggtgagaggc	aaggcatgag	agggcaagtt	tggtgtggac	agatctgtgc	ctactttatt	240
actggagtaa	aagaaaacaa	agttcattga	tgtcgaagga	tatatacagt	gtagaaaatt	300
a						301

<210> 285

<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 285
acatcaccat gatcggatcc cccacccatt atacgttgta tgtttacata aatactcttc 60
aatgatcatt agtgttttaa aaaaaatact gaaaactcct tctgcatccc aatctctaac 120
caggaaagca aatgctatct acagacctgc aagccctccc tcaaacnaaa ctatttctgg 180
attaaatatg tctgacttct tttgaggtca cactgactagg caaatgctat ttacgatctg 240
caaaagctgt ttgaagagtc aaagccccca tgtgaacacg atttctggac cctgtaacag 300
t 301

<210> 286
<211> 301
<212> DNA
<213> Homo sapien

<400> 286
taccactgca ttccagcctg ggtgacagag tgagactccg tctccaaaaa aaactttgct 60
tgtatattat ttttgcccta cagtggatca ttctagtagg aaaggacagt aagatttttt 120
atcaaaatgt gtcattgccag taagagatgt tatattcttt tctcatttct tccccacca 180
aaaataagct accatatagc ttataagtct caaatttttg ccttttacta aaatgtgatt 240
gtttctgttc attgtgtatg cttcatcacc tatattagga aaattccatt tttcccttg 300
t 301

<210> 287
<211> 301
<212> DNA
<213> Homo sapien

<400> 287
tacagatctg ggaactaaat attaaaaatg agtgtggctg gatatatgga gaatgttggg 60
cccagaagga acgtagagat cagatattac aacagctttg ttttgagggg tagaaatatg 120
aaatgatattg gttatgaacg cacagttagg gcagcagggc cagaatcctg accctctgcc 180
ccgtgggtat ctctcccca gcttggtctg ctcattgtat cacagtattc cattttgttt 240
gttgcattgc ttgtgaagcc atcaagattt tctcgtctgt tttcctctca ttggtaatgc 300
t 301

<210> 288
<211> 301
<212> DNA
<213> Homo sapien

<400> 288
gtacacctaa ctgcaaggac agctgaggaa tgtaatgggc agccgctttt aaagaagtag 60
agtcaatagg aagacaaatt ccagttccag ctcagtctgg gtatctgcaa agctgcaaaa 120
gatcttttaa gacaatttca agagaatatt tccttaaagt tggcaatttg gagatcatac 180
aaaagcatct gcttttgtga tttaatttag ctcactctgg cactggaaga atccaaacag 240
tctgccttaa ttttggtatg atgcatgatg gaaattcaat aatttagaaa gttaaaaaaa 300
a 301

<210> 289
<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 289

```
ggtacactgt ttccatgtta tgttttctaca cattgctacc tcagtgtctc tggaaactta      60
gcttttgatg tctccaagta gtccaccttc atttaactct ttgaaactgt atcatctttg      120
ccaagtaaga gtggtggcct atttcagctg ctttgacaaa atgactggct cctgacttaa      180
cgttctataa atgaatgtgc tgaagcaaag tgcccatggg ggcggcgaan aagagaaaga      240
tgtgttttgt tttggactct ctgtggtccc ttccaatgct gtgggtttcc aaccagnnga      300
a                                                                                   301
```

<210> 290

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 290

```
acactgagct cttcttgata aatatacaga atgcttggca tatacaagat tctatactac      60
tgactgatct gttcatttct ctcacagctc ttaccccca aagcttttcc accctaagtg      120
ttctgacctc cttttctaata cacagtaggg atagaggcag anccacctac aatgaacatg      180
gagttctatc aagaggcaga aacagcacag aatccagtt ttaccattcg ctagcagtgc      240
tgcttgaac aaaaacattt ctccatgtct cattttcttc atgcctcaag taacagtgag      300
a                                                                                   301
```

<210> 291

<211> 301

<212> DNA

<213> Homo sapien

<400> 291

```
caggtaccaaa tttcttctat cctagaaaca tttcatttta tgttgttgaa acataacaac      60
tatatcagct agattttttt tctatgcttt acctgctatg gaaaatttga cacattctgc      120
tttactcttt tgtttatagg tgaatcacia aatgtatttt tatgtattct gtagttcaat      180
agccatggct gtttacttca tttaatttat ttagcataaa gacattatga aaaggcctaa      240
acatgagctt cacttcccca ctaactaatt agcatctggt atttcttaac cgtaatgcct      300
a                                                                                   301
```

<210> 292

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 292

```

accttttagt agtaatgtct aataataaat aagaaatcaa ttttataagg tccatatagc      60
tgtattaaat aatttttaag tttaaaagat aaaataccat catttttaat gttggtattc      120
aaaaccaaag natataaccg aaaggaaaaa cagatgagac ataaaatgat ttgcnagatg      180
ggaaatatag tasttyatga atgttnatta aattccagtt ataatagtgg ctacacactc      240
tcactacaca cacagacccc acagtcctat atgccacaaa cacatttcca taacttgaaa      300
a                                                                                   301

```

```

<210> 293
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 293
ggtagcaagt gctggtgcca gcctgttacc tgtttctact gaaaagtctg gctaagtctc      60
ttgtgtagtc acttctgatt ctgacaatca atcaatcaat ggcctagagc actgactggt      120
aacacaaacg tcaactagcaa agtagcaaca gctttaagtc taaatacaaa gctgttctgt      180
gtgagaattt tttaaaaggc tacttgtata ataacccttg tcatttttaa tgtacctcgg      240
ccgcgaccac gctaagccga attctgcaga tatccatcac actggcggcc gctcgagcat      300
g                                                                                   301

```

```

<210> 294
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 294
tgaccataaa caatatacac tagctatctt tttaactgtc catcattagc accaatgaag      60
attcaataaaa attaccttta ttcacacatc tcaaaacaat tctgcaaatt cttagtgaag      120
tttaactata gtcacaganc ttaaataatc acattgtttt ctatgtctac tgaaaataag      180
ttcactactt ttctgggata ttctttacaa aatcttatta aaattcctgg tattatcacc      240
ccaattata cagtagcaca accaccttat gtagttttta catgatatagct ctgtagaggt      300
t                                                                                   301

```

```

<210> 295
<211> 305
<212> DNA
<213> Homo sapien

```

```

<400> 295
gtactctttc tctccctccc tctgaattta attctttcaa cttgcaattt gcaaggatta      60
cacatttcac tgtgatgtat attgtgttgc aaaaaaaaaa gtgtctttgt ttaaaattac      120
ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccactcttga      180
actggtagaa aaacrtctga agagctagtc tatcagcatc tgacaggaga attggatggt      240
tctcagaacc atttcacca gacagcctgt ttctatcctg ttttaataaat tagtttgggt      300
tctct                                                                                   305

```

```

<210> 296
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 296
aggtactatg ggaagctgct aaaataatat ttgatagtaa aagtatgtaa tgtgctatct      60

```



```

cacctagtag taaactaaaa ataaactgaa actttatgga atctgaagtt attttccttg      120
attaataga attaataaac caatatgagg aaacatgaaa ccatgcaatc tactatcaac      180
tttgaaaaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataagtcatt      240
tgtcattact ataaatttta aaatctgtta ataagatggc ctatagggag gaaaaagggg      300
c                                                                                   301

```

<210> 297

<211> 300

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(300)

<223> n = A,T,C or G

<400> 297

```

actgagtttt aactggacgc caagcaggca aggctggaag gttttgctct ctttgtgcta      60
aaggttttga aaaccttgaa ggagaatcat ttgacaaga agtacttaag agtctagaga      120
acaaagangt gaaccagctg aaagctctcg ggggaanctt acatgtgttg ttaggcctgt      180
tccatcattg ggagtgact ggccatccct caaaatttgt ctgggctggc ctgagtggtc      240
accgcacctc ggccgcgacc acgctaagcc gaattctgca gatatccatc acactggcgg      300

```

<210> 298

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 298

```

tatggggttt gtcacccaaa agctgatgct gagaaaggcc tccctggggc ccctcccgcg      60
ggcatctgag agacctgggtg ttccagtgtt tctggaaatg ggtcccagtg ccgccggctg      120
tgaagctctc agatcaatca cggaaggggc ctggcggtgg tggccacctg gaaccaccct      180
gtctgtctcg ttacatttc actaycaggt tttctctggg cattacnatt tgttccccta      240
caacagtgac ctgtgcattc tgctgtggcc tgctgtgtct gcaggtggct ctgagcgagg      300
t                                                                                   301

```

<210> 299

<211> 301

<212> DNA

<213> Homo sapien

<400> 299

```

gttttgagac ggagtttcac tcttggtgcc cagactggac tgcaatggca gggctctctgc      60
tactgcacc ctctgcctcc caggttcgag caattctcct gcctcagcct cccaggtagc      120
tgggattgca ggctcagccc accataccca gctaattttt ttgtattttt agtagagacg      180
gagtttggcc atgttggcc gctggctctca aactcctgac ctcaagcgac ctgcctgcct      240
cggcctccca aagtgtctgga attataggca tgagtcaaca cgcccagcct aaagatattt      300
t                                                                                   301

```

<210> 300

<211> 301

<212> DNA

<213> Homo sapien

<400> 300

attcagtttt atttgcctgcc ccagtatctg taaccaggag tgccacaaaa tcttgccaga	60
tatgtcccac acccactggg aaaggctccc acctggctac ttcctctatc agctgggtca	120
gctgcattcc acaaggttct cagcctaata agtttacta cctgccagtc tcaaaactta	180
gtaaagcaag accatgacat tccccacgg aaatcagagt ttgccccacc gtcttggtac	240
tataaagcct gcctctaaca gtccttgctt cttcacacca atccccagcg catccccat	300
g	301

<210> 301

<211> 301

<212> DNA

<213> Homo sapien

<400> 301

ttaaattttt gagaggataa aaaggacaaa taatctagaa atgtgtcttc ttcagtctgc	60
agaggacccc aggtctccaa gcaaccacat ggtaagggc atgaataatt aaaagttggt	120
gggaactcac aaagaccctc agagctgaga caccacacac agtgggagct cacaaagacc	180
ctcagagctg agacaccac aacagtggga gtcacaaaag accctcagag ctgagacacc	240
cacaacagca cctcgttcag ctgccacatg tgtgaataag gatgcaatgt ccagaagtgt	300
t	301

<210> 302

<211> 301

<212> DNA

<213> Homo sapien

<400> 302

aggtacacat ttagcttggt gtaaatgact cacaaaactg attttaaaat caagttaatg	60
tgaattttga aaattactac ttaatcctaa ttcacaataa caatggcatt aaggtttgac	120
ttgagttggt tcttagtatt atttatggta aataggctct taccacttgc aaataactgg	180
ccacatcatt aatgactgac tteccagtaa ggctctctaa ggggtaagta ggaggatcca	240
caggatttga gatgctaagg cccagagat cgtttgatcc aaccctctta ttttcagagg	300
g	301

<210> 303

<211> 301

<212> DNA

<213> Homo sapien

<400> 303

aggtaccaac tgtggaaata ggtagaggat cattttttct ttccatatca actaagttgt	60
atattgtttt ttgacagttt aacacatctt cttctgtcag agattctttc acaatagcac	120
tggtaatggg aactaccgct tgcattgtaa aaatgggtgt ttgtgaaatg atcataggcc	180
agtaatgggt atgtttttct aactgatctt ttgctcgttc caaagggacc tcaagacttc	240
catcgatttt atatctgggg tctagaaaag gagttaatct gttttccctc ataaattcac	300
c	301

<210> 304

<211> 301

<212> DNA

<213> Homo sapien

<400> 304

acatggatgt tattttgcag actgtcaacc tgaatttgta tttgcttgac attgcctaata	60
tattagtttc agtttcagct taccactttt ttgtctgcaa catgcaraas agacagtgcc	120
cttttttagtg tatcatatca ggaatcatct cacattgggt ttgtgccatta ctggtgcagt	180
gactttcagc cacttgggta aggtggagtt ggccatatgt ctccactgca aaattactga	240

ttttcctttt gtaattaata agtgtgtgtg tgaagattct ttgagatgag gtatatatct 300
c 301

<210> 305
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 305
gangtacagc gtggtcaagg taacaagaag aaaaaaatgt gagggtgcatc ctgggatgag 60
caggggggaca gacctggaca gacacgttgt catttgctgc tgtgggtagg aaaatgggag 120
taaaggagga gaaacagata caaaatctcc aactcagtat taaggatttc tcatgcctag 180
aatattggta gaaacaagaa tacattcata tggcaaataa ctaaccatgg tggacaacaaa 240
ttctgggatt taagttggat accaangaaa ttgtattaaa agagctgttc atggaataag 300
a 301

<210> 306
<211> 8
<212> PRT
<213> Homo sapien

<400> 306
Val Leu Gly Trp Val Ala Glu Leu
1 5

<210> 307
<211> 637
<212> DNA
<213> Homo sapien

<400> 307
acaggggratg aagggaaagg gagaggatga ggaagccccc ctggggattt ggtttgggtcc 60
ttgtgatcag gtggtctatg gggcttatcc ctacaaagaa gaatccagaa atagggggcac 120
attgaggaat gatacttgag cccaaagagc attcaatcat tgttttattt gccttmtttt 180
cacaccattg gtgagggagg gattaccacc ctgggggttat gaagatgggt gaacacccca 240
cacatagcac cggagatatg agatcaacag tttcttagcc atagagattc acagcccaga 300
gcaggaggac gcttgcacac catgcaggat gacatggggg atgcgctcgg gattgggtgtg 360
aagaagcaag gactgttaga ggcaggcttt atagtaacaa gacgggtggg caaactctga 420
tttccgtggg ggaatgtcat ggtcttgctt tactaagttt tgagactggc aggtagtga 480
actcattagg ctgagaacct tgtggaatgc acttgaccca sctgatagag gaagtagcca 540
gggtgggagcc tttccagtg ggtgtgggac atatctggca agattttgtg gcactcctgg 600
ttacagatac tggggcagca aataaaactg aatcttg 637

<210> 308
<211> 647
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(647)
<223> n = A,T,C or G

<400> 308

acgattttca	ttatcatgta	aatcgggtca	ctcaaggggc	caaccacagc	tgggagccac	60
tgctcagggg	aaggttcata	tgggactttc	tactgcccac	ggttctatac	aggatataaa	120
ggngcctcac	agtatagatc	tggtagcaaa	gaagaagaaa	caaacactga	tctctttctg	180
ccacccctct	gacccttttg	aactcctctg	accctttaga	acaagcctac	ctaatatctg	240
ctagagaaaa	gaccaacaac	ggcctcaaag	gatctcttac	catgaaggtc	tcagctaatt	300
cttggctaag	atgtgggttc	cacattaggt	tctgaatatg	gggggaaggg	tcaatttgct	360
cattttgtgt	gtggataaaag	tcaggatgcc	caggggccag	agcagggggc	tgcttgcttt	420
gggaacaatg	gctgagcata	taaccatagg	ttatggggaa	caaaacaaca	tcaaagtcac	480
tgtatcaatt	gccatgaaga	cttgagggac	ctgaatctac	cgattcatct	taaggcagca	540
ggaccagttt	gagtggcaac	aatgcagcag	cagaatcaat	ggaaacaaca	gaatgattgc	600
aatgtccttt	ttttctcct	gcttctgact	tgataaaagg	ggaccgt		647

<210> 309

<211> 460

<212> DNA

<213> Homo sapien

<400> 309

actttatagt	ttaggctgga	cattggaaaa	aaaaaaaagc	cagaacaaca	tgtgatagat	60
aatatgattg	gctgcacact	tccagactga	tgaatgatga	acgtgatgga	ctattgtatg	120
gagcacatct	tcagcaagag	ggggaaatac	tcatcatttt	tggccagcag	ttgtttgatc	180
accaaaccatc	atgccagaat	actcagcaaa	ccttcttagc	tcttgagaag	tcaaagtcag	240
ggggaattta	ttcctggcaa	ttttaattgg	actccttatg	tgagagcagc	ggctaccag	300
ctggggtggt	ggagcgaacc	cgtcactagt	ggacatgcag	tggcagagct	cctggtaacc	360
acctagagga	atacacaggc	acatgtgtga	tgccaagcgt	gacacctgta	gcaactcaaat	420
ttgtcttggt	tttgtctttc	ggtgtgtaag	attcttaagt			460

<210> 310

<211> 539

<212> DNA

<213> Homo sapien

<400> 310

acgggactta	tcaaataaag	ataggaaaag	aagaaaactc	aaatattata	ggcagaaatg	60
ctaaagggtt	taaaatatgt	caggattgga	agaaggcatg	gataaagaac	aaagttcagt	120
taggaaagag	aaacacagaa	ggaagagaca	caataaaaag	cattatgtat	tctgtgagaa	180
gtcagacagt	aagattttgt	ggaaatgggt	tggtttgttg	tatggtatgt	attttagcaa	240
taatctttat	ggcagagaaa	gctaaaatcc	tttagcttgc	gtgaatgatc	acttgcctgaa	300
ttcctcaagg	taggcatgat	gaaggagggt	ttagaggaga	cacagacaca	atgaactgac	360
ctagatagaa	agccttagta	tactcagcta	ggaatagtga	ttctgagggc	acactgtgac	420
atgattatgt	cattacatgt	atggtagtga	tggggatgat	aggaagggaag	aacttatggc	480
atattttcac	ccccacaaaa	gtcagttaaa	tattgggaca	ctaaccatcc	aggtcaaga	539

<210> 311

<211> 526

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(526)

<223> n = A,T,C or G

<400> 311

caaatttgag	ccaatgacat	agaattttac	aatcaagaa	gcttattctg	gggccatttc	60
ttttgacgtt	ttctctaaac	tactaaagag	gcattaatga	tccataaatt	atattatcta	120
catttacagc	atttaaaatg	tgttcagcat	gaaatattag	ctacagggga	agctaaataa	180

attaaacatg	gaataaagat	ttgtccttaa	atataatcta	caagaagact	ttgatatttg	240
tttttcacaa	gtgaagcatt	cttataaagt	gtcataacct	ttttggggaa	actatgggaa	300
aaaatgggga	aactctgaag	ggttttaagt	atcttacctg	aagctacaga	ctccataacc	360
tctctttaca	gggagctcct	gcagccccta	cagaaatgag	tggctgagat	tcttgattgc	420
acagcaagag	cttctcatct	aaaccctttc	cctttttagt	atctgtgtat	caagtataaa	480
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<210> 312

<211> 500

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(500)

<223> n = A,T,C or G

<400> 312

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tcatttctga	aagcagttga	gccactttat	tccaaagtac	actgcagatg	ttcaaactct	120
ccatttctct	ttcccttcca	cctgccagtt	ttgctgactc	tcaacttgtc	atgagtgtaa	180
gcattaagga	cattatgctt	cttcgattct	gaagacaggc	cctgctcatg	gatgactctg	240
gcttcttagg	aaaatatttt	tcttccaaaa	tcagtaggaa	atctaaactt	atccctctt	300
tgcagatgtc	tagcagcttc	agacatttgg	ttaagaacct	atgggaaaaa	aaaaaatcct	360
tgctaattgt	gtttcctttg	ttaaccanga	ttcttatttg	nctggtatag	aatatcagct	420
ctgaacgtgt	ggtaaagatt	tttgtgtttg	aatataggag	aatcagttt	gctgaaaagt	480
tagtcttaat	tatctattgg					500

<210> 313

<211> 718

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(718)

<223> n = A,T,C or G

<400> 313

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tgatgataca	gaggtgagaa	ataagaaagg	ctgctgactt	taccatctga	ggccacacat	120
ctgctgaaat	ggagataatt	aacatcacta	gaaacagcaa	gatgacaata	taatgtctaa	180
gtagtacat	gtttttgcac	atttccagcc	cttttaaata	tccacacaca	caggaagcac	240
aaaaggaagc	acagagatcc	ctgggagaaa	tgcccgccg	ccatcttggg	tcacgatga	300
gcctcgccct	gtgcctgntc	ccgcttgga	gggaaggaca	ttagaaaatg	aattgatgtg	360
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aactggggag	gagataccac	ggggcagagg	tcaggattct	ggccctgctg	cctaactgtg	600
cgttatacca	atcatttcta	tttctaccct	caaacaagct	gtngaataac	tgacttacgg	660
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<210> 314

<211> 358

<212> DNA

<213> Homo sapien

<400> 314

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caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg tgtagtccaa 180
gctctcggtg gtccagccac tgtgaaacat gctcccttta gattaacctc gtggacgctc 240
ttgttgtatt gctgaactgt agtgccctgt attttgcttc tgtctgtgaa ttctgttget 300
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<210> 315

<211> 341

<212> DNA

<213> Homo sapien

<400> 315

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gacccccatt ctgaagatgt ctggaacctc taccagcagg atgatgatag cccaatgac 180
agtccaccagc tccccgacca gccggatata gtccttaggg gtcatgtagg ctctctgaag 240
tagcttctgc tgtaagaggg tgttgtcccc ggggctcgtg cggttattgg tcttgggctt 300
gagggggcgg tagatgcagc acatggtgaa gcagatgatg t 341

<210> 316

<211> 151

<212> DNA

<213> Homo sapien

<400> 316

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cattcagga gctctggttg caatattagt t 151

<210> 317

<211> 151

<212> DNA

<213> Homo sapien

<400> 317

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atcttcattt atctctggcc ttaacctggt ctctgagggc tgcggccagc agatcccagg 120
ccagggctct gttcttgcca cacctgcttg a 151

<210> 318

<211> 151

<212> DNA

<213> Homo sapien

<400> 318

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gctgcagget ggagtgtctt tattcctggc gggagaccgc acattccact gctgaggctg 120
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<210> 319

<211> 151

<212> DNA

<213> Homo sapien

<400> 319

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taagattggg tttatgtgat tttagtgggt a 151

<210> 320
<211> 150
<212> DNA
<213> Homo sapien

<400> 320
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gagcggctgc cctttttttt tttttttttg ggggggaatt tttttttttt aatagttatt 120
gagtgttcta cagcttacag taaataccat 150

<210> 321
<211> 151
<212> DNA
<213> Homo sapien

<400> 321
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taggggtggca ttgtaaccag ctatggcata ggtgttaacc aaaggctgag taaacatggg 120
tgctctgag aatcaaagt cttcatacac t 151

<210> 322
<211> 151
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(151)
<223> n = A,T,C or G

<400> 322
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tttgggcttg gtcagtttgc cacagggctt ggagatgggt acagtcttct ggcattcggc 120
attgtgcagg gctcgttca nacttccagt t 151

<210> 323
<211> 151
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(151)
<223> n = A,T,C or G

<400> 323
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nagactcant tactaccag tttgtggtt twtgggagaa atgtaactgg acagttagct 120
gttcaatyaa aaagacactt anccatgtg g 151

<210> 324
<211> 461
<212> DNA
<213> Homo sapien

<220>

<221> misc_feature
<222> (1)...(461)
<223> n = A,T,C or G

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agagttacta cgaatcccat cttggttcca gctatatcac tgacagcatg gtagaagact 180
gcgaacctca cttctagact ttacacgttg gacgaaacgg gttcagaaac tgccaggggc 240
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cacacaaatg caatagttag tcaactgcatt ttacactgaa ccaaagctaa acccggtgtt 360
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aaaaacgcac aagagcccc tgcctgcccc agctgangca c 461

<210> 325
<211> 400
<212> DNA
<213> Homo sapien

<400> 325
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<210> 326
<211> 1215
<212> DNA
<213> Homo sapien

<400> 326
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aaaaaaaaa aaaaa 1215

<210> 327
<211> 220

<212> PRT

<213> Homo sapien

<400> 327

Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met
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 Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val
 20 25 30
 Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly
 35 40 45
 Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu
 50 55 60
 Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala
 65 70 75 80
 Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp
 85 90 95
 Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn
 100 105 110
 Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro
 115 120 125
 Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys
 130 135 140
 Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly
 145 150 155 160
 Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro
 165 170 175
 Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala
 180 185 190
 Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys
 195 200 205
 Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 210 215 220

<210> 328

<211> 234

<212> DNA

<213> Homo sapien

<400> 328

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 atccgcagtg ggtgctgtca gccacacact gtttcagaa ctctacacc atcgggctgg 180
 gcctgcacag tcttgaggcc gaccaagagc caggagacca gatggtggag gcca 234

<210> 329

<211> 77

<212> PRT

<213> Homo sapien

<400> 329

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 20 25 30
 Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Thr
 35 40 45
 His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu
 50 55 60

Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala
 65 70 75

<210> 330
 <211> 70
 <212> DNA
 <213> Homo sapien

<400> 330
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 gctgcagcca 70

<210> 331
 <211> 22
 <212> PRT
 <213> Homo sapien

<400> 331
 Gln His Asn Gly Pro Ile Pro Ser Leu Thr Pro Pro Ser Gly Ser Leu
 1 5 10 15
 Val Ser Gly Ser Cys Ser
 20

<210> 332
 <211> 2507
 <212> DNA
 <213> Homo sapien

<400> 332
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<210> 333

<211> 3030

<212> DNA

<213> Homo sapien

<400> 333

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<212> DNA

<213> Homo sapien

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<211> 2984

<212> DNA

<213> Homo sapien

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 <212> PRT
 <213> Homo sapien

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 35 40 45
 Val Ile Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala
 50 55 60
 Pro Glu Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln
 65 70 75 80
 Val Lys Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln
 85 90 95
 Leu Ser Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala
 100 105 110
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 Ala Phe Trp
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 <212> PRT
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 <212> PRT
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<211> 483
<212> DNA
<213> Homo sapien
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<212> DNA
<213> Homo sapien
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<210> 342

<211> 592

<212> DNA

<213> Homo sapien

<400> 342

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cctggcaggt aaaccaatgc caagagagtg atggaaacca ttggcaagac tttgttgatg	180
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<211> 382

<212> DNA

<213> Homo sapien

<400> 343

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<210> 344

<211> 536

<212> DNA

<213> Homo sapien

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<211> 251

<212> DNA

<213> Homo sapien

<400> 345

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gcgtggggcca ggaaatcaca tcctacactg cccaggagcc agacacattt atggaacaga	180
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<210> 346

<211> 282

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

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<400> 346

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<210> 347

<211> 201

<212> DNA

<213> Homo sapien

<220>

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<222> (1)...(201)

<223> n = A,T,C or G

<400> 347

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<210> 348

<211> 251

<212> DNA

<213> Homo sapien

<400> 348

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<210> 349

<211> 251

<212> DNA

<213> Homo sapien

<400> 349

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cagaagggtc tgaactctac gtgttaccag agaacataat gcaattcatg cattccactt	180
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<210> 350

<211> 908

<212> DNA

<213> Homo sapien

<400> 350

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cggttggaat tgctctggtt atgatgacag agaaaatgat ctcttctctt gtgacaccaa	180
cacctgtaaa tttgatgggg aatgtttaag aattggagac actgtgactt gcgtctgtca	240
gttcaagtgc aacaatgact atgtgcctgt gtgtgggtcc aatggggaga gctaccagaa	300
tgagtgttac ctgcgacagg ctgcatgcaa acagcagagt gagatacttg tgggtgtcaga	360
aggatcatgt gccacagtcc atgaaggctc tggagaaact agtcaaaagg agacatccac	420
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gtgtaatatt gactgttctc aaaccaactt caatccccct tgcgcttctg atgggaaatc	540
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catgtctttg ggtcgatgtc aagataacac aactacaact actaagtctg aagatgggca	660
ttatgcaaga acagattatg cagagaatgc taacaaatta gaagaaagtg ccagagaaca	720
ccacatacct tgtccggaac attacaatgg cttctgcatg catgggaagt gtgagcattc	780
tatcaatatg caggagccat cttgcagggt tgatgctggt tatactggac aacactgtga	840
aaaaaaggac tacagtgttc tatacgttgt tcccggctct gtacgatttc agtatgtctt	900
aatcgacg	908

<210> 351

<211> 472

<212> DNA

<213> Homo sapien

<400> 351

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cattaacttg attttaaaat cagwtttgyg agtcatttac cacaagctaa atgtgtacac	180
tatgataaaa acaaccattg tattcctgtt tttctaaaca gtccataattt ctaacactgt	240
atatatcctt cgacatcaat gaactttgtt ttcttttact ccagtaataa agtaggcaca	300
gatctgtcca caacaaactt gccctctcat gccttgctc tcaccatgct ctgctccagg	360
tcagccccct tttggcctgt ttgttttgtc aaaaacctaa tctgttctt gcttttcttg	420
gtaatatata tttagggaag atgttgcttt gccacacac gaagcaaagt aa	472

<210> 352

<211> 251

<212> DNA

<213> Homo sapien

<400> 352

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tgtggataag gccaggtcaa tggctgcaag catgcagaga aagaggtaca tcggagcgtg	120
caggctgcgt tccgtcctta cgatgaagac cagcatgcag tttccaaaca ttgccactac	180
atacatggaa aggaggggga agccaacca gaaatgggct ttctctaate ctgggatacc	240
aataagcaca a	251

<210> 353
 <211> 436
 <212> DNA
 <213> Homo sapien

<400> 353
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 gtatccaaaa gcaaaacagc agatatacaa aattaaagag acagaagata gacattaaca 180
 gataaggcaa cttatacatt gacaatccaa atccaataca tttaaacatt tgggaaatga 240
 gggggacaaa tggaagccar atcaaatttg tgtaaaacta ttcagtatgt ttcccttgct 300
 tcatgtctga raaggctctc ccttcaatgg ggatgacaaa ctccaaatgc cacacaaatg 360
 ttaacagaat actagattca cactggaacg ggggtaaaga agaaattatt ttctataaaa 420
 gggctcctaa tgtagt 436

<210> 354
 <211> 854
 <212> DNA
 <213> Homo sapien

<400> 354
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 atcaggggacc accctttggg ttgatatttt gcttaatctg catcttttga gtaagatcat 180
 ctggcagtag aagctgttct ccaggtagat ttctctagct catgtacaaa aacatcctga 240
 aggactttgt caggtgcctt gctaaaagcc agatgcgttc ggcacttctt tggctctgagg 300
 ttaattgcac acctacaggc actgggctca tgctttcaag tattttgtcc tcactttagg 360
 gtgagtgaag gatcccatc ataggagcag ttgggagaga tcatataaaa gctgactctt 420
 gagtacatgc agtaatgggg tagatgtgtg tgggtgtctc tcattcctgc aagggtgctt 480
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 caatatggaa ggctctaatt tgcccatatt tgaaataata attcagcttt ttgtaataca 660
 aaataacaaa ggattgagaa tcatgggtgc taatgtataa aagacccagg aaacataaat 720
 atatcaactg cataaatgta aaatgcatgt gacccaagaa ggccccaag tggcagacaa 780
 cattgtaccc attttccctt ccaaaatgtg agcggcgggc ctgctgcttt caaggctgtc 840
 acacgggatg tcag 854

<210> 355
 <211> 676
 <212> DNA
 <213> Homo sapien

<400> 355
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 atccacaagt catacctgga tgtcagcgaa gagggcacgg aggcagcagc agccactggg 180
 gacagcatcg ctgtaaaaag cctaccaatg agagctcagt tcaaggcgaa ccaccccttc 240
 ctgttcttta taaggcacac tcataccaac acgatcctat tctgtggcaa gcttgccctt 300
 ccctaatacag atggggttga gtaaggctca gagttgcaga tgagggtgcag agacaatcct 360
 gtgactttcc cacggccaaa aagctgttca cacctcacgc acctctgtgc ctgagtttgc 420
 tcatctgcaa aataggtcta ggatttctc caaccatttc atgagttgtg aagctaaggc 480
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 ggtgtctcat ttgagtgtg tccagtgcac tgatcaagtc aatgagtaaa attttaaggg 600
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 gcttaagaa aaccag 676

<210> 356

<211> 574
 <212> DNA
 <213> Homo sapien

<400> 356
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 caagcttccc atttgtagat ctgagtgcct atgagtatct gacacctgtt cctctcttca 180
 gtctcttagg gaggtctaaa tctgtctcag gtgtgctaag agtgccagcc caaggkgttc 240
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 ttcttctgtc tctgcctaga ctggaataaa aagccaatct ctctcgtggc acaggggaagg 420
 agatacaagc tcgtttacat gtgatagatc taacaaaggc atctaccgaa gtctgggtctg 480
 gatagacggc acaggagct cttaggtcag cgtgtgtgtg tggaggacat tcttgagtcc 540
 agctttgcag cctttgtgca acagtacttt ccca 574

<210> 357
 <211> 393
 <212> DNA
 <213> Homo sapien

<400> 357
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 aagccacaac caaracttga ttttatcaac aaaaaccctt aaatataaac ggsaaaaaag 180
 atagatataa ttattccagt ttttttaaaa cttaaaarat attccattgc cgaattaara 240
 araarataag tggtatatgg aaagaagggc attcaagcac actaaaraaa cctgaggkaa 300
 gcataatctg tacaaaatta aactgtcctt tttggcattt taacaaattt gcaacgktct 360
 tttttttctt tttctgtttt tttttttttt tac 393

<210> 358
 <211> 630
 <212> DNA
 <213> Homo sapien

<400> 358
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 gcatagagta gggaagctaa tccagcacag ggaggtcaca gagacatccc taagggaagt 180
 gagtttaaac tgagagaagc aagtgtctaa actgaaggat gtgttgaga agaagggaga 240
 gtagaacaat ttgggcagag ggaaccttat agaccctaag gtgggaagg tcaaagaact 300
 gaaagagagc tagaacagct ggagccgttc tccggtgtaa agaggagtca aagagataag 360
 attaaagatg tgaagattaa gatcttggtg gcattcaggg attggcactt ctacaagaaa 420
 tcaactgaagg gagtaatgtg acattacttt tcaactcagg atggccattc taactccagg 480
 gggtagactg gactaggtaa gactggaggc aggtagacct cttctaaggc ctgcatagat 540
 gaaagacaaa aataagtggg gaaattcagg ggatagttaa aatcagtagg acttaatgag 600
 caagccagag gttcctccac aacaaccagt 630

<210> 359
 <211> 620
 <212> DNA
 <213> Homo sapien

<400> 359
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 taattaaaaa atgctactaa tatagaaaat ttataatcag aaaaaataat attcagggag 120
 ctaccagaaa gaataaagtg ctctgccagt tattaaagga ttactgtctg tgaattaaat 180
 atggcattcc ccaagggaaa tagagagatt cttctggatt atgttcaata tttatttcac 240

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aggattaact gtttttaggaa cagatataaa gcttcgccac ggaagagatg gacaaagcac      300
aaagacaaca tgatacctta ggaagcaaca ctaccctttc aggcataaaa tttggagaaa      360
tgcaacatta tgcttcatga ataatatgta gaaagaagggt ctgatgaaaa tgacatcctt      420
aatgtaagat aactttataa gaattctggg tcaaataaaa ttctttgaag aaaacatcca      480
aatgtcattg acttatcaaa tactatcttg gcatataacc tatgaaggca aaactaaaca      540
aacaataaagc tcacacaaa caaaaccatc aacttatttt gtattctata acatacgaga      600
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<210> 360

<211> 431

<212> DNA

<213> Homo sapien

<400> 360

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tactcatcat ttttggccag cagttgtttg atcaccaaac atcatgccag aatactcagc      180
aaaccttctt agctcttgag aagtcaaagt ccgggggaat ttattcctgg caattttaat      240
tggtactcctt atgtgagagc agcggctacc cagctggggg ggtggagcga acccgtcact      300
agtggacatg cagtggcaga gctcctggta accacctaga ggaatacaca ggcacatgtg      360
tgatgccaaag cgtgacacct gtagcactca aatttgtctt gtttttgtct ttcggtgtgt      420
agattcttag t

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<210> 361

<211> 351

<212> DNA

<213> Homo sapien

<400> 361

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ttgggtcttc tgggtctctg ccaagtttcc cagccactcg agggagaaat atcgggaggt      180
ttgacttctt ccggggcttt cccgagggct tcaccgtgag ccctgcggcc ctacgggctg      240
caatcctgga ttcaatgtct gaaacctcgc tctctgacct ctggacttct gagggcgtca      300
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<210> 362

<211> 463

<212> DNA

<213> Homo sapien

<400> 362

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ccccggtcac agaaatgacc aggttgggtg ttttcaggtg ccagtgtggt gtcagcagct      180
cgtaaaggat ttccgcgtcc gtgtcgcagg acagacgtat atacttcctt ttcttcccca      240
gtgtctcaaa ctgaatatcc ccaaaggcgt cggtaggaaa ttcttgggtg tgtttcttgt      300
agttccattt ctacttttgg ttgatctggg tgccttccat gtgctggctc tgggcatagc      360
cacacttgca cacattctcc ctgataagca cgatggtgtg gacaggaagg aaggatttca      420
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<210> 363

<211> 653

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

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<223> n = A,T,C or G

<400> 363

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ntgggccctg	gagctgggat	gacattgagt	ttgagctgct	gacctgggat	gaggaaggag	540
attttgagag	tccntggtcc	agaattccat	ttaccttctg	ggccagatac	caccagaatg	600
cccgtccag	attccctcag	acctttgcgc	gtcccattat	tggtcstggt	ggt	653

<210> 364

<211> 401

<212> DNA

<213> Homo sapien

<400> 364

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aaaacaaggt	ggatagatct	agaattgtaa	cattttaaga	aaaccatagc	atttgacaga	180
tgagaaagct	caattataga	tgcaaagtta	taactaaact	actatagtag	taaagaaata	240
catttcacac	ccttcataata	aattcactat	cttggtctga	ggcactccat	aaaatgtatc	300
acgtgcatag	taaatcttta	tatttgctat	ggcgttgac	tagaggactt	ggactgcaac	360
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<210> 365

<211> 356

<212> DNA

<213> Homo sapien

<400> 365

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taccagagca	tcaagtctct	gcagcaggtc	attcttgggt	aaagaaatga	cttccacaaa	180
ctctccatcc	cctggctttg	gcttcggcct	tgcgttttcg	gcatcatctc	cgttaatggt	240
gactgtcacg	atgtgtatag	tacagtttga	caagcctggg	tccatacaga	ccgctggaga	300
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<210> 366

<211> 1851

<212> DNA

<213> Homo sapien

<400> 366

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tcacttctt	taagcctttg	tgactcttcc	tctgatgtca	gctttaagtc	tggttctgga	180
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ttggatcagt	gccatgttcc	agcaacatta	acgcacattc	atcttctctg	cattgtacgg	660
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<210> 367

<211> 668

<212> DNA

<213> Homo sapien

<400> 367

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accrtataag	agcagtgcct	tggccattaa	tttatctttc	attrtagaca	gcrtagtgya	180
gagtgggtatt	tccatactca	tctggaatat	ttggatcagt	gccatgttcc	agcaacatta	240
acgcacattc	atcttctctg	cattgtacgg	cctgtcagta	ttagacccaa	aaacaaatta	300
catatcttag	gaattcaaaa	taacattcca	cagctttcac	caactagtta	tatttaaagg	360
agaaaaactca	tttttatgcc	atgtattgaa	atcaaaacca	cctcatgctg	atatagtttg	420
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gcagtcctat	gagagtgaga	agacttttta	ggaaattgta	gtgcactagc	tacagccata	600
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aaaaaaaa						668

<210> 368

<211> 1512

<212> DNA

<213> Homo sapien

<400> 368

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ggagaccacg	acgactctgc	tatgaagaca	ctcaggagca	agatgggcaa	gtgggtgccg	420
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gccttcatgg	agcccaggta	ccacgtccgt	ggagaagatc	tggacaagct	ccacagagct	660
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aacaagaagg	acaagcaaaa	gaggactgct	ctacatctgg	cctctgccaa	tggaattca	780
gaagtagtaa	aactcstgct	ggacagacga	tgtcaactta	atgtccttga	caacaaaaag	840
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<210> 369

<211> 1853

<212> DNA

<213> Homo sapien

<400> 369

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<210> 370

<211> 2184

<212> DNA

<213> Homo sapien

<400> 370

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<210> 371

<211> 1855

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

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<223> n = A,T,C or G

<400> 371

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<210> 372

<211> 1059

<212> DNA

<213> Homo sapien

<400> 372

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<211> 1155

<212> DNA

<213> Homo sapien

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<211> 2000

<212> DNA

<213> Homo sapien

<400> 374

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 <212> DNA
 <213> Homo sapien

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 aatggtgata atggattaat tcctcaaaag aagagcagaa cacctgaaaa tcagcaattt 1380
 cctgacaacg aaagtgaaga gtatcacaga atttgcgat tagtttctga ctacaaagaa 1440
 aaacagatgc caaaatactc ttctgaaaac agcaaccag aacaagactt aaagctgaca 1500
 tcagaggaag agtcacaaag gcttgagggc agtgaaaatg gccagccaga gaaaagatct 1560
 caagaaccag aaataaataa ggatggtgat agagagctag aaaattttat ggctatcgaa 1620
 gaaatgaaga agcacggaag tactcatgtc ggattcccag aaaacctgac taatggtgac 1680
 actgctggca atggtgatga tggattaatt cctccaagga agagcagAAC acctgaaagc 1740
 cagcaatttc ctgacactga gaatgaagag tatcacagt acgaacaaaa tgatactcag 1800
 aagcaatttt gtgaagaaca gaacactgga atattacacg atgagattct gattcatgaa 1860
 gaaaagcaga tagaagtggg tgaaaaaatg aattctgagc tttctcttag ttgtaagaaa 1920
 gaaaagaca tcttgcatga aaatagtacg ttgcgggaag aaattgccat gctaagactg 1980
 gagctagaca caatgaaaca tcagagccag ctaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2040

<210> 376
 <211> 329
 <212> PRT
 <213> Homo sapien

<400> 376
 Met Asp Ile Val Val Ser Gly Ser His Pro Leu Trp Val Asp Ser Phe
 1 5 10 15
 Leu His Leu Ala Gly Ser Asp Leu Leu Ser Arg Ser Leu Met Ala Glu
 20 25 30
 Glu Tyr Thr Ile Val His Ala Ser Phe Ile Ser Cys Ile Ser Ser Ser
 35 40 45
 Leu Asp Gly Gln Gly Glu Arg Gln Glu Gln Arg Gly His Phe Trp Arg
 50 55 60

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Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Glu Val Gln Val
65          70          75          80
Val Leu Pro Leu Leu Pro Leu Leu Gln Gly Ser Gly Lys Ser Asn Val
          85          90          95
Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr
          100          105          110
His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp
          115          120          125
Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp
          130          135          140
Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser
145          150          155          160
Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys
          165          170          175
Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala
          180          185          190
Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly
          195          200          205
Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr
          210          215          220
Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr
225          230          235          240
Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu
          245          250          255
Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys
          260          265          270
Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu
          275          280          285
Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu
          290          295          300
Glu Gln Asn Val Asp Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu
305          310          315          320
Ser Met Leu Phe Leu Val Ile Ile Met
          325

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<210> 377
<211> 148
<212> PRT
<213> Homo sapien

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<220>
<221> VARIANT
<222> (1)...(148)
<223> Xaa = Any Amino Acid

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<400> 377
Met Thr Xaa Pro Ser Trp Ser Pro Gly Thr Thr Ser Val Glu Lys Ile
1          5          10          15
Trp Thr Ser Ser Thr Glu Leu Pro Trp Trp Gly Lys Val Pro Arg Lys
          20          25          30
Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Xaa Asp Lys
          35          40          45
Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu
          50          55          60
Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp
65          70          75          80
Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp
          85          90          95

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125

Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro
 100 105 110
 Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp
 115 120 125
 Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser
 130 135 140
 Lys Asn Lys Val
 145

<210> 378
 <211> 1719
 <212> PRT
 <213> Homo sapien

<400> 378
 Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
 1 5 10 15
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
 20 25 30
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
 35 40 45
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
 50 55 60
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
 65 70 75 80
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
 85 90 95
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
 100 105 110
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
 115 120 125
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
 130 135 140
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
 145 150 155 160
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
 165 170 175
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
 180 185 190
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
 195 200 205
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
 210 215 220
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
 225 230 235 240
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
 245 250 255
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
 260 265 270
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
 275 280 285
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
 290 295 300
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
 305 310 315 320
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
 325 330 335
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His Val

				340				345					350				
Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Leu	Lys	Ile		
		355					360					365					
Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Asn	Val	Ser	Arg	Thr	Arg	Asn	Lys		
	370				375						380						
Pro	Arg	Thr	His	Met	Val	Val	Glu	Val	Asp	Ser	Met	Pro	Ala	Ala	Ser		
385					390						395				400		
Ser	Val	Lys	Lys	Pro	Phe	Gly	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp	Cys		
				405					410					415			
Cys	Arg	Cys	Phe	Pro	Cys	Cys	Arg	Glu	Ser	Gly	Lys	Ser	Asn	Val	Gly		
			420					425					430				
Thr	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Ser	Lys		
		435					440					445					
Met	Gly	Lys	Trp	Cys	Arg	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser	Gly		
	450					455					460						
Lys	Ser	Asn	Val	Gly	Ala	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys		
465					470					475				480			
Thr	Leu	Arg	Asn	Lys	Met	Gly	Lys	Trp	Cys	Cys	His	Cys	Phe	Pro	Cys		
				485					490					495			
Cys	Arg	Gly	Ser	Gly	Lys	Ser	Lys	Val	Gly	Ala	Trp	Gly	Asp	Tyr	Asp		
			500					505					510				
Asp	Ser	Ala	Phe	Met	Glu	Pro	Arg	Tyr	His	Val	Arg	Gly	Glu	Asp	Leu		
		515					520					525					
Asp	Lys	Leu	His	Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val	Pro	Arg	Lys	Asp		
	530					535					540						
Leu	Ile	Val	Met	Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys	Gln		
545					550					555				560			
Lys	Arg	Thr	Ala	Leu	His	Leu	Ala	Ser	Ala	Asn	Gly	Asn	Ser	Glu	Val		
				565					570					575			
Val	Lys	Leu	Leu	Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp	Asn		
			580					585					590				
Lys	Lys	Arg	Thr	Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp	Glu		
		595					600					605					
Cys	Ala	Leu	Met	Leu	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro	Asp		
	610					615					620						
Glu	Tyr	Gly	Asn	Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys		
625					630					635					640		
Leu	Met	Ala	Lys	Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser	Lys		
			645						650					655			
Asn	Lys	His	Gly	Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val	His	Glu	Gln	Lys		
			660					665									

805 810 815
 Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn
 820 825 830
 Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe
 835 840 845
 Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser
 850 855 860
 Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn
 865 870 875 880
 Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu
 885 890 895
 Glu Gly Ser Glu Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile
 900 905 910
 Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn
 915 920 925
 Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro
 930 935 940
 Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu
 945 950 955 960
 Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe
 965 970 975
 Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His
 980 985 990
 Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser
 995 1000 1005
 Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu
 1010 1015 1020
 Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His
 1025 1030 1035 1040
 Gln Ser Gln Leu Pro Arg Thr His Met Val Val Glu Val Asp Ser Met
 1045 1050 1055
 Pro Ala Ala Ser Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met
 1060 1065 1070
 Gly Lys Trp Cys Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys
 1075 1080 1085
 Ser Asn Val Gly Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr
 1090 1095 1100
 Leu Arg Ser Lys Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys
 1105 1110 1115 1120
 Arg Gly Ser Gly Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp
 1125 1130 1135
 Ser Ala Met Lys Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His
 1140 1145 1150
 Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp
 1155 1160 1165
 Gly Asp Tyr Asp Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg
 1170 1175 1180
 Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val
 1185 1190 1195 1200
 Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys
 1205 1210 1215
 Lys Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly
 1220 1225 1230
 Asn Ser Glu Val Val Lys Leu Leu Asp Arg Arg Cys Gln Leu Asn
 1235 1240 1245
 Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys
 1250 1255 1260
 Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro

1265 1270 1275 1280
 Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr
 1285 1290 1295
 Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp
 1300 1305 1310
 Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Val
 1315 1320 1325
 His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala
 1330 1335 1340
 Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala
 1345 1350 1355 1360
 Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn
 1365 1370 1375
 Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr
 1380 1385 1390
 Ala Val Ser Ser His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr
 1395 1400 1405
 Lys Glu Lys Gln Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu
 1410 1415 1420
 Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly
 1425 1430 1435 1440
 Ser Glu Asn Ser Gln Pro Glu Lys Met Ser Ser Gln Glu Pro Glu Ile Asn
 1445 1450 1455
 Lys Asp Gly Asp Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser
 1460 1465 1470
 Asn Asn Val Gly Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly
 1475 1480 1485
 Asn Gly Asp Asn Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu
 1490 1495 1500
 Asn Gln Gln Phe Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys
 1505 1510 1515 1520
 Glu Leu Val Ser Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser
 1525 1530 1535
 Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu
 1540 1545 1550
 Ser Gln Arg Leu Glu Gly Ser Glu Asn Gly Gln Pro Glu Lys Arg Ser
 1555 1560 1565
 Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Leu Glu Asn Phe
 1570 1575 1580
 Met Ala Ile Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe
 1585 1590 1595 1600
 Pro Glu Asn Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly
 1605 1610 1615
 Leu Ile Pro Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro
 1620 1625 1630
 Asp Thr Glu Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln
 1635 1640 1645
 Lys Gln Phe Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile
 1650 1655 1660
 Leu Ile His Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser
 1665 1670 1675 1680
 Glu Leu Ser Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn
 1685 1690 1695
 Ser Thr Leu Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr
 1700 1705 1710
 Met Lys His Gln Ser Gln Leu
 1715

<210> 379
 <211> 656
 <212> PRT
 <213> Homo sapien

<400> 379
 Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
 1 5 10 15
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
 20 25 30
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
 35 40 45
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
 50 55 60
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
 65 70 75 80
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
 85 90 95
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
 100 105 110
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
 115 120 125
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
 130 135 140
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
 145 150 155 160
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
 165 170 175
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
 180 185 190
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
 195 200 205
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
 210 215 220
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
 225 230 235 240
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
 245 250 255
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
 260 265 270
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
 275 280 285
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
 290 295 300
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
 305 310 315 320
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
 325 330 335
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val
 340 345 350
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile
 355 360 365
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu
 370 375 380
 Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys
 385 390 395 400
 Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu
 405 410 415

Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn
 420 425 430
 Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro
 435 440 445
 Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu
 450 455 460
 Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu
 465 470 475 480
 Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp
 485 490 495
 Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu
 500 505 510
 Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys
 515 520 525
 Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly
 530 535 540
 Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser
 545 550 555 560
 Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr
 565 570 575
 His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln
 580 585 590
 Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln
 595 600 605
 Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys
 610 615 620
 Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile
 625 630 635 640
 Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu
 645 650 655

<210> 380

<211> 671

<212> PRT

<213> Homo sapien

<400> 380

Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
 1 5 10 15
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
 20 25 30
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
 35 40 45
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
 50 55 60
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
 65 70 75 80
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
 85 90 95
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
 100 105 110
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
 115 120 125
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
 130 135 140
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
 145 150 155 160
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala

165 170 175
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
 180 185 190
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
 195 200 205
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
 210 215 220
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
 225 230 235 240
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
 245 250 255
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
 260 265 270
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
 275 280 285
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
 290 295 300
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
 305 310 315 320
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
 325 330 335
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val
 340 345 350
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile
 355 360 365
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu
 370 375 380
 Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys
 385 390 395 400
 Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu
 405 410 415
 Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn
 420 425 430
 Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro
 435 440 445
 Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu
 450 455 460
 Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu
 465 470 475 480
 Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp
 485 490 495
 Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu
 500 505 510
 Asn Gly Gln Pro Glu Lys Arg Ser Gln Glu Pro Glu Ile Asn Lys Asp
 515 520 525
 Gly Asp Arg Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys Lys
 530 535 540
 His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly Ala
 545 550 555 560
 Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser Arg
 565 570 575
 Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr His
 580 585 590
 Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln Asn
 595 600 605
 Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln Ile
 610 615 620
 Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys Lys

625		630		635		640
Glu Lys Asp Ile Leu	His Glu Asn Ser Thr	Leu Arg Glu Glu Ile	Ala			
	645		650		655	
Met Leu Arg Leu Glu	Leu Asp Thr Met Lys His Gln Ser Gln	Leu				
	660		665		670	

<210> 381
 <211> 251
 <212> DNA
 <213> Homo sapien

<400> 381
 ggagaagcgt ctgctggggc aggaaggggt ttccctgccc tctcacctgt ccctcaccaa 60
 ggtaacatgc ttcccctaag ggtatcccaa cccaggggcc tcaccatgac ctctgagggg 120
 ccaatatccc aggagaagca ttggggagtt gggggcaggt gaaggacca ggactcacac 180
 atcctggggc tccaaggcag aggagagggt cctcaagaag gtcaggagga aaatccgtaa 240
 caagcagtca g 251

<210> 382
 <211> 3279
 <212> DNA
 <213> Homo sapiens

<400> 382
 cttctctgcag ccccatgct ggtgaggggc acgggcagga acagtggacc caacatggaa 60
 atgctggagg gtgtcaggaa gtgatcgggc tctggggcag ggaggagggg tggggagtgt 120
 cactgggagg ggacatcctg cagaaggtag gagtgcagaa acaccgctg caggggaggg 180
 gagagccctg cggcacctgg gggagcagag ggagcagcac ctgcccaggc ctgggaggag 240
 gggcctggag ggcgtgagga ggagcaggg ggctgcatgg ctggagttag ggatcagggg 300
 cagggcgaga tagggcctca cacagggaag agaggggccc tctgcaggg cctcacctgg 360
 gccacaggag gacactgctt ttctctgag gagtgcaggag ctgtggatgg tgcaggacag 420
 aagaaggaca gggcctggct caggtgtcca gaggctgtcg ctggcttccc tttgggatca 480
 gactgcaggg agggagggcg gcagggttgt ggggggagtg acgatgagga tgacctgggg 540
 gtggctccag gccttgcccc tgccctgggc ctcaccagc ctcctcaca gtctcctggc 600
 cctcagtctc tcccctccac tccatcctcc atctggcctc agtgggtcat tctgatcact 660
 gaactgacca tcccacgcc tgcccaggg cctccatggc tcccacatgc cctggagagg 720
 ggacatctag tcagagagta gtccctgaaga ggtggcctct gcgatgtgcc tgtgggggca 780
 gcacctgca gatggtccc gcccctatcc tgctgacctg tctgcaggga ctgtcctcct 840
 ggaccttgcc ccttgctgag gagctggacc ctgaagtccc ctcctccatag gccaagactg 900
 gagccttggt cctctgtgtg gactccctgc ccatattctt gtgggagtgg gttctggaga 960
 catttctgtc tgttcttgag agctgggaat tgcctcagc catctgcctg cgcggttctg 1020
 agagatggag ttgcctaggc agttattggg gccaatcttt ctcactgtgt ctctcctcct 1080
 ttacccttag ggtgattctg ggggtccact tgcctgtaat ggtgtgcttc aaggtatcac 1140
 atcatggggc cctgagccat gtgccctgcc tgaaaagcct gctgtgtaca ccaaggtggt 1200
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<210> 383

<211> 154

<212> PRT

<213> Homo sapiens

<400> 383

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      20              25              30
His Cys Phe Ser Ser Glu Glu Ser Gly Ala Val Asp Gly Ala Gly Gln
      35              40              45
Lys Lys Asp Arg Ala Trp Leu Arg Cys Pro Glu Ala Val Ala Gly Phe
      50              55              60
Pro Leu Gly Ser Asp Cys Arg Glu Gly Gly Arg Gln Gly Cys Gly Gly
      65              70              75              80
Ser Asp Asp Glu Asp Asp Leu Gly Val Ala Pro Gly Leu Ala Pro Ala
      85              90              95
Trp Ala Leu Thr Gln Pro Pro Ser Gln Ser Pro Gly Pro Gln Ser Leu
      100             105             110
Pro Ser Thr Pro Ser Ser Ile Trp Pro Gln Trp Val Ile Leu Ile Thr
      115             120             125
Glu Leu Thr Ile Pro Ser Pro Ala His Gly Pro Pro Trp Leu Pro Asn
      130             135             140
Ala Leu Glu Arg Gly His Leu Val Arg Glu
      145             150

```

<210> 384
 <211> 557
 <212> DNA
 <213> Homo sapiens

<400> 384
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 ggggaagggt cccttttgca ttgccaagt ccataaccat gagcactact ctaccatggg 180
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 ctctgtagag agcagcattc ccaggaccc tggaaacagt tggcactgta aggtgcttgc 360
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 ccttcttatt tatgtgaaca actgtttgtc tttttttgta tcttttttaa actgtaaagt 480
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 aaaaaaaaaa aaaaaaa 557

<210> 385
 <211> 337
 <212> DNA
 <213> Homo sapiens

<400> 385
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 tctcaaagcc atctgctgtc ttcgagtacg gacacatcat cactcctgca ttgttgatca 180
 aaacgtggag gtgcttttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240
 tatcagacag gtccagtttc cgcaccaaca cctgctgggt ccctgtcgtg gtctggatct 300
 ctttggccac caattcccc ttttccacat cccggca 337

<210> 386
 <211> 300
 <212> DNA
 <213> Homo sapiens

<400> 386
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 gccgcctcgg ccagaggggt gggcgcgggg ctgcctctac cggctggcgg ctgtaactca 120
 gcgaccttgg ccgaaggct cttagcaagg cccaccgacc ccagccgcgg cggcgggcggc 180
 gcggactttg cccggtgtgt ggggcggagc ggactgctg tccgcggacg ggcagcgaag 240
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<210> 387
 <211> 537
 <212> DNA
 <213> Homo sapiens

<400> 387
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 tgaaccagga cgggttctg ggcggctgaa aggggcaagg aggcaaggac cccgtctctc 180
 ccacggatgg ggagagggca ggaggagacc cagccaagt ccttttctc agcactgagg 240
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 gcggcccagc acttctcag acacaacttc ttcctgctgc tccagtcgtg gggatcatca 360
 cttacccacc cccaagtgc aagaccaaact cttccagctg ccccttctgt gtttccctgt 420
 gtttgcgtga gctgggcatg tctccaggaa ccaagaagcc ctcagcctgg tgtagtctcc 480
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<210> 388
<211> 520
<212> DNA
<213> Homo sapiens

<400> 388
aggataat ttaaaccaat caaatgaaaa aaacaaacaa acaaaaaagg aaatgtcatg 60
tgaggtaa ccagtttgca ttccccta atgtggaaaa taagaggact actcagcact 120
gtttgaagat tgctcttct acagcttctg agaatttgtt tatttcactt gccaaagtga 180
ggacccccct cccaacatgc ccagcccccac ccctaagcat ggtcccttgt caccaggcaa 240
ccaggaaact gctacttgtg gacctcacca gagaccagga gggtttggtt agctcacagg 300
acttccccca cccagaaga ttagcatccc atactagact catactcaac tcaactaggc 360
tcatactcaa ttgatgggta ttagacaatt ccatttcttt ctgggttatta taaacagaaa 420
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atgaacttgt cttattttaa tgggtgggtt tttttctggt 520

<210> 389
<211> 365
<212> DNA
<213> Homo sapiens

<400> 389
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aacgactttc caaataatct caccagcgcc ttccagctca ggcgtcctag aagcgtcttg 180
aagcctatgg ccagctgtct ttgtgttccc tctcacccgc ctgtcctcac agctgagact 240
cccaggaaac cttcagacta ctttctctg ccttcagcaa ggggcgttgc ccacattctc 300
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gggag 365

<210> 390
<211> 221
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(221)
<223> n = A,T,C or G

<400> 390
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gctctangag tctgancnga ntcgttgccc cantntgaca naaggaaagg cggagcttat 180
tcaaaagtcta gagggagtgg aggagttaag gctggatttc a 221

<210> 391
<211> 325
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(325)
<223> n = A,T,C or G

<400> 391


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tagccagggc actgctgcc aacagccagtc cnnataccat catgtnaccc ggtgngctct 180
naanttngat ntccanagcc ctacccatcn tagttctgct ctcccaccgg ntaccagccc 240
cactgcccag gaatcctaca gccagtaccc tgtcccgcag tctctacctt ccagtacgat 300
gagacctccg gctactacta tgacc                                     325

```

<210> 392

<211> 277

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(277)

<223> n = A,T,C or G

<400> 392

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atattgttta actccttcct ttatatcttt taacattttc atggngaaa gttcacatct 60
agtctcactt nggcnagn gn ctctacttg agtctcttcc ccggcctggn ccagtngnaa 120
antaccanga accgncatgn cttanaa ncttggttn tgggttnntc aatgactgca 180
tgcagtgcac caccctgtcc actacgtgat gctgtaggat taaagtctca cagtgggcgg 240
ctgaggatac agcgccgcgt cctgtgttgc tggggaa                                     277

```

<210> 393

<211> 566

<212> DNA

<213> Homo sapiens

<400> 393

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actagtcag tgtggtggaa ttcgcgccg cgctgcagga caggtcagct gtctggctca 60
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ttgcccggaa cactgcagag acaatgctgt gagtttccaa ccttagccca tctgcgggca 180
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ttctgcctca atgtttactg tgcccttgtt tttgctagtt tgtgttgttg aaaaaaaaaa 480
cattctctgc ctgagtttta atttttgtcc aaagttattt taatctatac aattaaaagc 540
ttttgcctat caaaaaaaaa aaaaaa                                     566

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<210> 394

<211> 384

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(384)

<223> n = A,T,C or G

<400> 394

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gcaggaggac cgggctttta ggagttttta gctgagtgtc actgtagacc ccaaatacca 180
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gaacatccag tttcctgata aggacgatgg gaaccagccc caggaccaa ttaccatcac 300
agggtacgaa aagaacacag aagctgccag gtagctata ctgagaattg tgggtgaact 360

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tgagcagatg gtttctgagg acgt

384

<210> 395

<211> 399

<212> DNA

<213> Homo sapiens

<400> 395

ggcaaaactg tgtgacctca ataagacctc gcagatccaa ggtcaagtat cagaagtgac 60
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ccagctactt gtctgcaatt gtatcttcaa gaataccctg gccatccctt tgactgacgt 300
caagtctctt ttggaaagcc tgggcatctc ctactacag acctctgacc atgggacggg 360
gcagcctggg gagaccatcc aatcccaaat aaaatgcac 399

<210> 396

<211> 403

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(403)

<223> n = A,T,C or G

<400> 396

tggagtnttc agtgcaaaca agccataaag cttcagtagc aaattactgt ctcacagaaa 60
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agacaaggac aacctgttcc ttcataactc tctagagaaa aaaaggagtt gttagtagat 180
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gttttagggga gggagtgagg gataaaagaa ggaaaaaaag aagagtgaga aaacctatct 360
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<210> 397

<211> 100

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

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<223> n = A,T,C or G

<400> 397

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tccatccccg ctcttggttg gtnacagaat gactgacaaa 100

<210> 398

<211> 278

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(278)

<223> n = A,T,C or G

<400> 398

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ccacctggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120
tcactactgt gcctcgacca gtgaggagag ctggaccgac agcgagggtg actcatcatg 180
ctccgggcag cccatccacc tgtggcagtt cctcaaggag ttgctactca agccccacag 240
ctatggccgc ttcattangt ggctcaacaa ggagaagg 278
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<210> 399

<211> 298

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(298)

<223> n = A,T,C or G

<400> 399

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ggggtgcnng catggagcgc atgggcgcgg gcctggggcca cggcatggat cgcgtgggct 120
ccgagatcga gcgcatgggc ctggtcatgg accgcatggg ctccgtggag cgcgtgggct 180
ccggcattga gcgcatgggc ccgctgggccc tcgaccacat ggctccanc attgancgca 240
tgggcccagac catggagcgc attggctctg gcgtggagcn catgggtgcc ggcgtggg 298
```

<210> 400

<211> 548

<212> DNA

<213> Homo sapiens

<400> 400

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acatcaacta cttcctcatt ttaaggtatg gcagttccct tcateccctt ttctgcctt 60
gtacatgtac atgtatgaaa ttctcttctc ttaccgaact ctctccacac atcacaagg 120
caaagaacca cacgcttaga agggtaagag ggcaccctat gaaatgaaat ggtgatttct 180
tgagtctctt ttttccacgt ttaagggggc atggcaggac ttagagttgc gagttaagac 240
tgcagagggc tagagaatta tttcatacag gctttgaggc caccatgtc acttatcccc 300
tataccctct caccatcccc ttgtctactc tgatgcccc aagatgcaac tgggcagcta 360
gttgggccca taattctggg cctttgttgt ttgttttaat tacttgggca tcccaggaag 420
ctttccagtg atctcctacc atgggcccc ctctgggat caagcccctc ccaggccctg 480
tccccagccc ctctgcccc agcccacccg cttgccttgg tgetcagccc tccatttggg 540
agcaggtt 548
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<210> 401

<211> 355

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(355)

<223> n = A,T,C or G

<400> 401

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tgatgtctcc aagtagtcca cttcatttta actctttgaa actgtatcat ctttgccaag 120
taagagtggg ggcctatttc agctgctttg acaaaatgac tggctcctga cttaacgttc 180
tataaatgaa tgtgtggaag caaagtgcc atggtggcgg cgaagaagan aaagatgtgt 240
ttgttttgg actctctgtg gtcccttcca atgctgnggg tttccaacca ggggaagggt 300
```

ccctttttgca ttgccaagtg ccataaccat gagcactact ctaccatggn tctgc 355

<210> 402

<211> 407

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(407)

<223> n = A,T,C or G

<400> 402

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tctcacatgc ggtggcatac ataggctcaa aataaaggaa tggagaaaaa tatttcaagc 120
aaatggaaaa cagaaaaaag caggtgttgc actcctactt tctgacaaaa cagactatgc 180
gaataaagat aaaaaagaga aggacattac aaagggtggtc ctgacctttg ataaatctca 240
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ttgtggagct tctccctgc agagagtccc tgatctccca aaatttggtt gagatgtaag 360
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<210> 403

<211> 303

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(303)

<223> n = A,T,C or G

<400> 403

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tcctaagcaa gagccatggc atggtgaaaa tgcaaaaagg gagtctggcc aatctacaaa 120
tagagaacaa gacctactca gtcataaaca aaaaggcaga caccaacatg gatctcatgg 180
gggattggat attgtaatta tagagcagga agatgacagt gatcgatcatt tggcacaaca 240
tcttaacaac gaccgaaacc cattattttac ataaacctcc attcggtaac catgttgaaa 300
gga 303

<210> 404

<211> 225

<212> DNA

<213> Homo sapiens

<400> 404

aagtgttaact tttaaaaatt tagtggattt tgaaaattct tagaggaaaag taaaggaaaa 60
attgttaatg cactcattta cctttacatg gtgaaagtcc tctcttgatc ctacaaacag 120
acatttttcca ctggtgtttc catagtgtgt aagtgtatca gatgtgttgg gcatgtgaat 180
ctccaagtgc ctgtgtaata aataaagtat ctttattttca ttcatt 225

<210> 405

<211> 334

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(334)

<223> n = A,T,C or G

<400> 405

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gagctgttat actgtgagtt ctactaggaa atcatcaaat ctgaggggtg tctggaggac 60
ttcaatacac ctccccccat agtgaatcag cttccagggg gtccagtcct tctccttact 120
tcatacccat cccatgccaa aggaagacct tccctccttg gctcacagcc ttctctagga 180
ttcccagtgct cccaggaca gagtgggtta tgttttcagc tccatccttg ctgtgagtgt 240
ctggtgcggt tgtgcctcca gcttctgctc agtgettcac ggacagtgtc cagcccatgt 300
cactctccac tctctcanng tggatcccac ccct 334
```

<210> 406

<211> 216

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(216)

<223> n = A,T,C or G

<400> 406

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gaaacaaaca cccaataaac tcggagtggc agactgacaa ctgtgagaca tgcacttgct 120
acnaaacaca aatttnatgt tgcacccttg tttctacacc tgtgggttat gacaaagaca 180
actgccaaaag aatnttcaag aaggaggact gccant 216
```

<210> 407

<211> 413

<212> DNA

<213> Homo sapiens

<400> 407

```
gctgacttgc tagtatcatc tgcattcatt gaagcacaag aacttcatgc cttgactcat 60
gtaaatgcaa taggattaaa aaataaattt gatatcacat ggaaacagac aaaaaatatt 120
gtacaacatt gcaccagtg tcagattcta cacctggcca ctcaggaagc aagagttaat 180
cccagaggtc tatgtcctaa tgtgttatgg caaatggatg tcatgcacgt accttcattt 240
ggaaaattgt catttgtcca tgtgacagtt gatacttatt cacatttcat atgggcaacc 300
tgccagacag gagaaagtct tcccatgtta aaagacattt attatcttgt ttctctgtca 360
tgggagtccc agaaaaagtt aaaacagaca atgggccagg ttctgtagta aag 413
```

<210> 408

<211> 183

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(183)

<223> n = A,T,C or G

<400> 408

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ggagctngcc ctcaattcct ccatntctat gttancatat ttaatgtctt ttgnnattaa 60
tncttaacta gttaatcctt aaagggetan ntaatcctta actagtcctt ccattgtgag 120
cattatcctt ccagtattcn ccttctnttt tattttactcc ttcttggtta cccatgtact 180
ntt 183
```

<210> 409

<211> 250

<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(250)
<223> n = A,T,C or G

<400> 409
cccacgcatg ataagctctt tatttctgta agtcctgcta ggaaatcatc aaatctgacg 60
gtgggttggg ggacctgaac aaacctcctg taattaatca gctttcagtt tctcccccta 120
gtccctcctt caacaacata ggaggatcct ccccttcttt ctgtcacgg ccttatctag 180
gcttccaggt gccccagga cagcgtgggc tatgtttaca gcgctcctt gctggggggg 240
ggcctatgct 250

<210> 410
<211> 306
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(306)
<223> n = A,T,C or G

<400> 410
ggctgggttg caagaatgaa atgaatgatt ctacagctag gacttaacct tgaaatggaa 60
agtcttgcaa tccatttgc aggatccgtc tgtgcacatg cctctgtaga gagcagcatt 120
cccagggacc ttggaaacag ttggcactgt aagggtgctt ctccccaaga cacatcctaa 180
aagggtgtgt aatggtgaaa accgcttctt tctttattgc cccttcttat ttatgtgaac 240
nactgggttg ctttttttgn atctttttta aactggaaaag ttcaattgng aaaatgaata 300
tctgct 306

<210> 411
<211> 261
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(261)
<223> n = A,T,C or G

<400> 411
agagatattn cttaggtnaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaagtgc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240
cttctctcaa ggngaggcaa a 261

<210> 412
<211> 241
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(241)

<223> n = A,T,C or G

<400> 412

```
gttcaatggt acctgacatt tctacaacac ccactcacc gatgtattcg ttgcccagtg 60
ggaacatacc agcctgaatt tggaaaaaat aattgtgttt cttgcccagg aaatactacg 120
actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggaggggag 180
ctggggagatt tcaactgggta cattgaattc caaaactacc cangcaatta cccagccaac 240
a                                                                 241
```

<210> 413

<211> 231

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(231)

<223> n = A,T,C or G

<400> 413

```
aactcttaca atccaagtga ctcatctgtg tgcttgaatc ctttccactg tctcatctec 60
ctcatccaag tttctagtac cttctctttg ttgtgaagga taatcaaact gaacaacaaa 120
aagtttactc tcctcatttg gaacctaaaa actctcttct tcctgggtct gagggctcca 180
agaatccttg aatcanttct cagatcattg gggacaccan atcaggaacc t          231
```

<210> 414

<211> 234

<212> DNA

<213> Homo sapiens

<400> 414

```
actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60
gatggagctg aaaacataac ccactctgtc ctggaggcac tgggaagcct agagaaggct 120
gtgagccaag gagggagggt ctctcttttg catgggatgg ggatgaagta aggagaggga 180
ctggaccccc tggaagctga ttcactatgg ggggagggtg attgaagtcc tcca      234
```

<210> 415

<211> 217

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(217)

<223> n = A,T,C or G

<400> 415

```
gcataggatt aagactgagt atcttttcta cattctttta actttctaag gggcacttct 60
caaaacacag accaggtagc aaatctccac tgctctaagg ntctcaccac cacttttctca 120
cacctagcaa tagtagaatt cagtcctact tctgaggcca gaagaatggt tcagaaaaat 180
antggattat aaaaaataac aattaagaaa aataatc          217
```

<210> 416

<211> 213

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature
<222> (1)...(213)
<223> n = A,T,C or G

<400> 416
atgcataatnt aaagganact gcctcgcttt tagaagacat ctggnctgct ctctgcatga 60
ggcacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120
cgaatgcaag gtgggttaatt gaaggccact aattgatgct caaatagaag gatattgact 180
atattggaac agatggagtc tctactacaa aag 213

<210> 417
<211> 303
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(303)
<223> n = A,T,C or G

<400> 417
nagtcttcag gcccatcagg gaagttcaca ctggagagaa gtcatacata tgtactgtat 60
gtgggaaagg ctttactctg agttcaaadc ttcaagccca tcagagagtc cacactggag 120
agaagccata caaatgcaat gagggtggga agagcttcag gagggattcc cattatcaag 180
ttcatctagt ggtccacaca ggagagaaac cctataaatg tgagatatgt gggaagggtc 240
tcantcaaag ttcgtatctt caaatccatc ngaaggncca cagtatanan aaacctttta 300
agt 303

<210> 418
<211> 328
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(328)
<223> n = A,T,C or G

<400> 418
tttttggcgg tgggtggggca gggacggggac angagtctca ctctgttgcc caggctggag 60
tgcacaggca tgatctcggc tcactacaac ccctgcctcc catgtccaag cgattcttgt 120
gcctcagcct tcctgtagc tagaattaca ggcacatgcc accacaccca gctagttttt 180
gtatttttag tagagacagg gtttcaccat gttggccagg ctggtctcaa actcctnacc 240
tcagnggtca ggctgggtct aaactcctga cctcaagtga tctgcccacc tcagcctccc 300
aaagtgctan gattacaggc cgtgagcc 328

<210> 419
<211> 389
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(389)
<223> n = A,T,C or G

<400> 419
cctcctcaag acggcctgtg gtccgcctcc cggcaaccaa gaagcctgca gtgccatatg 60


```
acccttgagc catggactgg agcctgaaag gcagcgtaca ccctgctect gatcttgctg 120
cttgtttcct ctctgtggct ccattcatag cacagttggt gactgaggc ttgtgcaggc 180
cgagcaaggc caagctggct caaagagcaa ccagtcaact ctgccacggg gtgccaggca 240
ccggttctcc agccaccaac ctcaactcgt cccgcaaatt gcacatcagt tcttctacce 300
taaaggtagg accaaagggc atctgtcttt ctgaagtctt ctgctctatc agccatcacg 360
tggcagccac tcnggctgtg tcgacgcgg 389
```

<210> 420

<211> 408

<212> DNA

<213> Homo sapiens

<400> 420

```
gttcctccta actcctgcca gaaacagctc tcctcaacat gagagctgca ccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttcc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcattggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg aagtgcctatg acaaacctgg caagcccc 408
```

<210> 421

<211> 352

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(352)

<223> n = A,T,C or G

<400> 421

```
gctcaaaaat ctttttactg atnngcatgg ctacacaatc attgactatt acggaggcca 60
gaggagaatg aggcctggcc tgggagccct gtgcctacta naagcacatt agattateca 120
ttcactgaca gaacaggtct tttttgggtc cttcttctcc accacnata acttgagtc 180
ctccttcttg aagattcttt ggcagttgtc tttgtcataa ccacacaggt tagaaacaag 240
ggtgcaacat gaaatttctg tttcgtagca agtgcattgc tcacaagttg gcangtctgc 300
cactccgagt ttattgggtg tttgtttcct ttgagatcca tgcatttctt gg 352
```

<210> 422

<211> 337

<212> DNA

<213> Homo sapiens

<400> 422

```
atgccaccat gctggcaatg cagcgggcgg tcgaaggcct gcatatccag cccaagctgg 60
cgatgatcga cggcaaccgt tgcccgaagt tgccgatgcc agccgaagcg gtggtcaagg 120
gcgatagcaa ggtgccggcg atcgcggcgg cgtcaatcct ggccaaggct agccgtgatc 180
gtgaaatggc agctgtcgaa ttgatctacc cgggttatgg catcggcggg cataagggtc 240
atccgacacc ggtgcacctg gaagccttgc agcggctggg gccgacgccg attcaccgac 300
gcttcttccg ccggtacggc tggcctatga aaattat 337
```

<210> 423

<211> 310

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature
<222> (1)...(310)
<223> n = A,T,C or G

<400> 423
gctcaaaaat ctttttactg atatggcatg gctacacaat cattgactat tagaggccag 60
aggagaatga ggcctggcct gggagccctg tgccactan aagcncatta gattatccat 120
tcaactgacag aacaggtcct ttttgggtcc tcttctcca ccacgatata cttgcagtc 180
tccttcttga agattctttg gcagttgtct ttgtcataac ccacaggtgt anaaacaagg 240
gtgcaacatg aaatttctgt ttcgtagcaa gtgcatgtct cacagttgtc aagtctgccc 300
tccgagttta 310

<210> 424
<211> 370
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(370)
<223> n = A,T,C or G

<400> 424
gctcaaaaat ctttttactg atagggcatg ctacacaatc attgactatt agaggccaga 60
ggagaatgag ggcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120
caactgacaga acaggtcctt tttgggtcct tcttctccac cacgatatac ttgcagtcct 180
ccttcttgaa gattcttttg cagttgtctt tgtcataacc cacaggtgta gaaacatcct 240
ggttgaatct cctggaactc cctcattagg tatgaaatag catgatgat tgcataaagt 300
cacgaagggtg gcaaagatca caacgctgcc cagganaaca ttcattgtga taagcaggac 360
tccgtcgacg 370

<210> 425
<211> 216
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(216)
<223> n = A,T,C or G

<400> 425
aattgctatn ntttattttg ccactcaaaa taattaccaa aaaaaaaaaa tnttaaataga 60
taacaacnca acatcaagggn aaananaaca ggaatggntg actntgcata aatnggccga 120
anattatcca ttatnttaag gggtgacttc aggntacagc acacagacaa acatgcccag 180
gaggntntca ggaccgctcg atgtntntg aggagg 216

<210> 426
<211> 596
<212> DNA
<213> Homo sapiens

<400> 426
cttccagtga ggataaccct gttgccccgg gccgaggttc tccattaggc tctgattgat 60
tggcagtcag tgatggaagg gtgttctgat cattccgact gcccgaaggg tcgctggcca 120
gctctctgtt ttgctgagtt ggcagtagga cctaatttgt taattaagag tagatggtga 180
gctgtccttg tatttttgatt aacctaatgg ccttcccagc acgactcgga ttcagctgga 240
gacatcacgg caacttttaa tgaaatgatt tgaagggccca ttaagaggca cttcccgtta 300

ttaggcagtt catctgcact gataacttct tggcagctga gctggtcgga gctgtggccc 360
aaacgcacac ttggcttttg gttttgagat acaactctta atcttttagt catgcttgag 420
ggtggatggc cttttcagct ttaacccaat ttgcaactgc ttggaagtgt agccaggaga 480
atacactcat atactcgtgg gcttagaggg cacagcagat gtcattggtc tactgcctga 540
gtcccgctgg tcccatccca ggaccttcca tcggcgagta cctgggagcc cgtgct 596

<210> 427

<211> 107

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(107)

<223> n = A,T,C or G

<400> 427

gaagaattca agttaggttt attcaaaggg cttacngaga atcctanacc caggncaccag 60
cccgaggagca gccttanaga gtcctgttt gactgccgg ctcagng 107

<210> 428

<211> 38

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(38)

<223> n = A,T,C or G

<400> 428

gaacttcena anaangactt tattcactat ttacatt 38

<210> 429

<211> 544

<212> DNA

<213> Homo sapiens

<400> 429

ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60
attgaagagc ggctgcagcc ctgcggttca gattaaaatc cgagaattgt atagacgccg 120
atatccacga actcttgaag gactttctga tttatccaca atcaaatacat cggttttcag 180
tttggatggt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactcgtt 240
gccttcact tcagttacac ctactcacc atcctctcct gttggttctg tgctgcttca 300
agatactaag cccacatttg agatgcagca gccatctccc ccaattctc ctgtccatcc 360
tgatgtgcag ttaaaaaatc tgccctttta tgatgtcctt gatgttctca tcaagcccac 420
gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttattt ttgctttgac 480
acctcaacaa gttagagaga tatgcatatc cagggatttt ttgccagggtg gtaggagaga 540
ttat 544

<210> 430

<211> 507

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(507)

<223> n = A,T,C or G

<400> 430

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cttatcncaa tggggctccc aaacttggt gtgcagtga aactccggg gaattttgaa 60
gaacactgac acccatcttc caccgacac ctctgattta attgggctgc agtgagaaca 120
gagcatcaat ttaaaaagct gcccgagaatg ttntcctggg cagcgttggtg atctttgccn 180
ccttcgtgac tttatgcaat gcatcatgct atttcatacc taatgaggga gttccaggag 240
attcaaccag gatgttttcta cncctgtggg ttatgacaaa gacaactgcc aaagaatntt 300
caagaaggag gactgcaagt atatcgtggt ggagaagaag gacccaaaaa agacctgttc 360
tgtcagtga tggataatct aatgtgcttc tagtaggcac agggctccca ggccaggcct 420
cattctcctc tggcctctaa tagtcaatga ttgtgtagcc atgcctatca gtaaaaagat 480
ttttgagcaa aaaaaaaaaa aaaaaaa
```

507

<210> 431

<211> 392

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(392)

<223> n = A,T,C or G

<400> 431

```
gaaaattcag aatggataaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60
aaacaagaaa gcacttatca ggaggactta caaatggaag tacactctan aaccatcatc 120
tatcatggct aaatgtgaga ttagcacagc tgtattatth gtacattgca aacacctaga 180
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtccctgggtt ttccaacaga 240
catcattcca gcattctgag attagggnga ttggggatca ttctggagtt ggaatgttca 300
acaaaagtga tgttgttagg taaaatgtac aacttctgga tctatgcaga cattgaaggt 360
gcaatgagtc tggctttttac tctgctgttt ct
```

392

<210> 432

<211> 387

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(387)

<223> n = A,T,C or G

<400> 432

```
ggtatccnta cataatcaaa tatagctgta gtacatgttt tcattggngt agattaccac 60
aaatgcaagg caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg 120
ngtagtccaa gctctcgga gtccagccac tngaaacat gctcccttta gattaacctc 180
gtggacnctn ttgttgnatt gtctgaactg tagngccctg tattttgctt ctgtctgnga 240
attctgttgc ttctggggca ttctcttngn atgcagagga ccaccacaca gatgacagca 300
atctgaattg ntccaatcac agctgcgatt aagacatact gaaatcgta aggaccggga 360
acaacgtata gaacactgga gtccttt
```

387

<210> 433

<211> 281

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(281)

<223> n = A,T,C or G

<400> 433

```
ttcaactagc anagaanact gcttcagggn gtgtaaaatg aaaggcttcc acgcagttat 60
ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120
caggcnctat ttgggttggc tggaggagct gtggaaaaca tggagagatt ggcgctggag 180
atcgccgtgg ctattcctcn ttgntattac accagnagg ntctctgtnt gccactgggt 240
tnnaaaaccg ntatacaata atgatagaat aggacacaca t 281
```

<210> 434

<211> 484

<212> DNA

<213> Homo sapiens

<400> 434

```
ttttaaaata agcatttagt gctcagtcct tactgagtag tctttctctc cctcctctctg 60
aatttaattc tttcaacttg caatttgcaa ggattacaca tttcactgtg atgtatattg 120
tggtgcaaaa aaaaaaaagt gtctttgttt aaaattactt gggttgtaga tccatcttgc 180
tttttcccca ttggaactag tcattaacct atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acaggtgaat tggatgggtc tcagaacctt ttcaccaga 300
cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca taacaaacct 360
tgctccaatc tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag taccatgtc 480
ttta 484
```

<210> 435

<211> 424

<212> DNA

<213> Homo sapiens

<400> 435

```
gcgccgtca gagcaggtea ctttctgcct tccacgtcct ccttcaagga agccccatgt 60
gggtagcttt caatctcgca ggttcttact cctctgcctc tataagctca aaccaccaa 120
cgatcgggca agtaaacccc ctccctcgcc gacttcggaa ctggcgagag ttcagcgag 180
atgggcctgt ggggaggggg caagatagat gagggggagc ggcattgggtc ggggtgacct 240
cttgagagaga ggaaaaaggc cacaagaggg gctgccaccg ccactaacgg agatggccct 300
ggtagagacc tttgggggtc tggaaacctc ggactcccca tgctctaact cccacactct 360
gctatcagaa acttaaaactt gaggattttc tctgtttttc actcgcaata aattcagagc 420
aac 424
```

<210> 436

<211> 667

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(667)

<223> n = A,T,C or G

<400> 436

```
accttgggaa nactctcaca atataaaggg tcgtagactt tactccaaat tccaaaaagg 60
tcttgcccat gtaatcctga aagttttccc aaggtagcta taaaatcctt ataagggtgc 120
agcctcttct ggaattcctc tgatttcaaa gtctcactct caagttcttg aaaacgaggg 180
cagttcctga aaggcaggta tagcaactga tcttcagaaa gaggaactgt gtgcaccggg 240
atgggctgcc agagtaggat aggattccag atgctgacac cttctggggg aaacagggct 300
gccaggtttg tcatagcact catcaaagtc cgttcaacgt ctgtgcttcg aatataaacc 360
```

tgttcatgtt tataggactc attcaagaat tttctatata tctttcttat atactctcca 420
agttcataat gctgctccat gccagctgg gtgagttggc caaatccttg tggccatgag 480
gattccttta tggggtcagt gggaaagggt tcaatgggac ttcggtctcc atgccgaaac 540
accaaagtca caaacttcaa ctcttggct agtacacttc ggtctagcca gaaaaaagc 600
agaaacaaga agccaaggct aaggcttgct gccctgccag gaggaggggt gcagctctca 660
tgttgag 667

<210> 437

<211> 693

<212> DNA

<213> Homo sapiens

<400> 437

ctacgtctca accctcattt ttaggtaagg aatcttaagt ccaaagatat taagtgactc 60
acacagccag gtaaggaaag ctggattggc acactaggac tctaccatac cgggttttgt 120
taaagctcag gttaggaggc tgataagctt ggaaggaact tcagacagct ttttcagatc 180
ataaaagata attcttagcc catgttcttc tccagagcag acctgaaatg acagcacagc 240
aggtaactct ctattttcac cctcttggct tctactctct ggcagtcaga cctgtgggag 300
gccatgggag aaagcagctc tctggatggt tgtacagatc atggactatt ctctgtggac 360
catttctcca ggttacccta ggtgtcacta ttgggggggac agccagcatc tttagctttc 420
atttgagttt ctgtctgtct tcagtagagg aaacttttgc tcttcacact tcacatctga 480
acacctaact gctgttgctc ctgaggtggt gaaagacaga tatagagctt acagtattta 540
tcctatttct aggcactgag ggctgtgggg taccttgtgg tgccaaaaca gatcctgttt 600
taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgttg gctctttacc 660
ctgcatcatg tgctctcttg gctgaaaatg acc 693

<210> 438

<211> 360

<212> DNA

<213> Homo sapiens

<400> 438

ctgcttatca caatgaatgt tctcctgggc agcgttgtga tctttgccac cttcgtgact 60
ttatgcaatg catcatgcta tttcatacct aatgagggag ttccaggaga ttcaaccagg 120
atgtttctac acctgtgggt tatgacaaag acaactgcc aagaatcttc aagaaggagg 180
actgcaagta tatctgttgg agaagaagga cccaaaaaag acctgttctg tcagtgaatg 240
gataatctaa tgtgcttcta gtaggcacag ggctcccagg ccaggcctca ttctcctctg 300
gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360

<210> 439

<211> 431

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(431)

<223> n = A,T,C or G

<400> 439

gttctnnta actcctgcc aaaacagctc tctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttct tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgacttttgt gtttcggcat ggagaccgaa 180
gtcccattga cacttttccc actgaccca taaaggaaac ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatataaaaa attcttgaat gactcctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgctga cgcggccgag 420
aatttagtag t 431

<210> 440

<211> 523

<212> DNA

<213> Homo sapiens

<400> 440

```
agagataaag cttagggtcaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaagtgc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagtccagc 240
cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300
actggaaaac tgctactatc tgtttttata tttctgttaa aatatatgag gctacagaac 360
taaaaattaa aacctctttg tgtcccttgg tcttggaaaca tttatgttcc ttttaaagaa 420
acaaaaatca aactttacag aaagatttga tgtatgtaat acatatagca gctcttgaag 480
tatatatatc atagcaaata agtcatctga tgagaacaag cta 523
```

<210> 441

<211> 430

<212> DNA

<213> Homo sapiens

<400> 441

```
gttctctcta actcctgcc aaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggtc tcttggttct gcttttttcc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgaccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
aatttagtag 430
```

<210> 442

<211> 362

<212> DNA

<213> Homo sapiens

<400> 442

```
ctaaggaatt agtagtggtc ccatcacttg tttggagtgt gctattctaa aagattttga 60
tttcttgga tgacaattat attttaactt tgggtgggga aagagttata ggaccacagt 120
cttcacttct gatacttgta aattaatctt ttattgcaact tgttttgacc attaagctat 180
atgtttagaa atggtcattt tacggaaaaa ttagaaaaat tctgataata gtgcagaata 240
aatgaattaa tgttttactt aatttatatt gaactgtcaa tgacaaataa aaattctttt 300
tgattatatt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360
tc 362
```

<210> 443

<211> 624

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(624)

<223> n = A,T,C or G

<400> 443

```
tttttttttt gcaacacaat atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60
```

```

ttgaaagaat taaattcaga ggaggggaga gaaagagtac tcagtaggga ctgagcacta 120
aatgcttatt ttaaaagaaa tgtaaagagc agaaagcaat tcaggctacc ctgccttttg 180
tgctggctag tactccggtc ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240
cccaaaccac agaaaatggg gtgaaattgg ccaactttct attaacttgg ctctctgttt 300
tataaaatat tgtgaataat atcacctact tcaaagggca gttatgaggc ttaaatgaac 360
taacgcctac aaacactta aacatagata acataggtgc aagtactatg tatctggtac 420
atggtaaaca tccttattat taaagtcaac gctaaaatga atgtgtgtgc atatgcta 480
agtacagaga gagggcactt aaaccaacta agggcctgga gggaagggtt cctggaaaga 540
ngatgcttgt gctgggtcca aatcttggtc tactatgacc ttggccaaat tatttaaact 600
ttgtccctat ctgctaaaca gatc
624

```

<210> 444

<211> 425

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(425)

<223> n = A,T,C or G

<400> 444

```

gcacatcatt nntcttgcatt tctttgagaa taagaagatc agtaaatagt tcagaagtgg 60
gaagctttgt ccaggcctgt gtgtgaaccc aatgttttgc ttagaaatag aacaagtaag 120
ttcattgcta tagcataaca caaaatttgc ataagtgggtg gtcagcaaatt ccttgaatgc 180
tgcttaattgt gagagggttg taaaatcctt tgtgcaacac tctaactccc tgaatgtttt 240
gctgtgctgg gacctgtgca tgccagacaa ggccaagctg gctgaaagag caaccagcca 300
cctctgcaat ctgccacctc ctgctggcag gatttgtttt tgcactctgt gaagagccaa 360
ggaggcacca gggcataagt gagtagactt atggtcgacg cggccgcgaa tttagtagta 420
gtaga
425

```

<210> 445

<211> 414

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(414)

<223> n = A,T,C or G

<400> 445

```

catgtttatg nttttggatt actttgggca cctagtgttt ctaaactcgtc tatcattcct 60
ttctgttttt caaaagcaga gatggccaga gtctcaacaa actgtatctt caagtctttg 120
tgaaattcctt tgcattgtggc agattatttg atgtagtctt cttaacttag catataaatc 180
tggtgtgttt cagataaatg aacagcaaaa tgtggtggaa ttaccatttg gaacattgtg 240
aatgaaaaat tgtgtctcta gattatgtaa caaataacta ttctctaacc attgatcttt 300
ggatttttat aatcctactc acaaatgact aggcctctcc tcttgatttt tgaagcagtg 360
tggtgtgctgg attgataaaa aaaaaaaag tcgacgcggc cgcgaattta gtag
414

```

<210> 446

<211> 631

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(631)

<223> n = A,T,C or G

<400> 446

```

acaaattaga anaaagtgcc agagaacacc acataccttg tccggaacat tacaatggct 60
tctgcatgca tgggaagtgt gagcattcta tcaatatgca ggagccatct tgcaggtgtg 120
atgctgggtta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttggtc 180
ccggtcctgt acgatttcag tatgtcttaa tcgcagctgt gattggaaca attcagattg 240
ctgtcatctg tgtggtggtc ctctgcatca caagggccaa actttaggta atagcattgg 300
actgagattt gtaaactttc caaccttcca ggaaatgccc cagaagcaac agaattcaca 360
gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420
taatctaaag ggagcatgtt tcacagtggc tggactaccg agagcttggg ctacacaata 480
cagtattata gacaaaagaa taagacaaga gatctacaca tgttgacctg catttggtgg 540
aatctacacc aatgaaaaca tgtactacag ctatatattga ttatgtatgg atatatattg 600
aatagtatac attgtcttga tgttttttct g                                     631

```

<210> 447

<211> 585

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(585)

<223> n = A,T,C or G

<400> 447

```

ccttgggaaa antntcacaa tataaagggt cgtagacttt actccaaatt ccaaaaagggt 60
cctggccatg taatcctgaa agttttccca aggtagctat aaaatcctta taagggtgca 120
gcctcttctg gaattcctct gatttcaaag tctcactctc aagttcttga aaacgagggc 180
agttcctgaa aggcaggtat agcaactgat cttcagaaag aggaactgtg tgcaccggga 240
tgggctgcca gagtaggata ggattccaga tgctgacacc ttctggggga aacagggctg 300
ccaggtttgt catagcactc atcaaagtcc ggtcaacgtc tgtgcttcga atataaacct 360
gttcattgtt ataggactca ttcaagaatt ttctatatct ctttcttata tactctccaa 420
gttcataatg ctgctccatg cccagctggg tgagttggcc aaatccttgt ggccatgagg 480
attcctttat ggggtcagtg ggaaagggtg caatgggact tcggtctcca tgccgaaaca 540
ccaaagtcac aaacttcaac tccttggtca gtacacttcg gtcta                                     585

```

<210> 448

<211> 93

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(93)

<223> n = A,T,C or G

<400> 448

```

tgctcgtggg tcattctgan nnccgaactg acctgccag ccctgccgan gggccnccat 60
ggctccctag tgcctggag agganggggc tag                                     93

```

<210> 449

<211> 706

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(706)

<223> n = A,T,C or G

<400> 449

```
ccaagttcat gctntgtgct ggacgctgga cagggggcaa aagcnnttgc tcgtgggtca 60
ttctgancac cgaactgacc atgccagccc tgccgatggc cctccatggc tccctagtgc 120
cctggagagg aggtgtctag tcagagagta gtccctggaag gtggcctctg ngaggagcca 180
cggggacagc atcctgcaga tggtcgggcg cgtcccatc gccattcagg ctgcgcaact 240
gttgggaagg gcgatcggcg cgggcctctt cgctattac ccagctggcg aaagggggat 300
gtgctgcaag gcgattaagt tgggtaacgc cagggttttc ccagtcncga cgttgtaaaa 360
cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcattgcacg 420
cgtacgtaag cttggatcct ctagagcggc cgctactac tactaaattc gcggccgcgt 480
cgacgtggga tccnactga gagagtggag agtgacatgt gctggacnct gtccatgaag 540
cactgagcag aagctggagg cacaacgcnc cagacactca cagctactca ggaggctgag 600
aacaggttga acctgggagg tggaggttgc aatgagctga gatcaggccn ctgcncceca 660
gcatggatga cagagtgaaa ctccatctta aaaaaaaaaa aaaaaa 706
```

<210> 450

<211> 493

<212> DNA

<213> Homo sapiens

<400> 450

```
gagacggagt gtcaactctgt tgcccaggct ggagtgcagc aagacactgt ctaagaaaaa 60
acagttttta aaggtaaaac aacataaaaa gaaatatcct atagtggaaa taagagagtc 120
aatgaggctt gagaacttta caaagggatc ttacagacat gtcgccaata tcaactgcatg 180
agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ggtacaattc 240
caagtcaggt agtgaatagg gtggaattaa actcaaatta atcctgccag ctgaaacgca 300
agagacactg tcagagagtt aaaaagttag ttctatccat gaggtgatcc cacagtcttc 360
tcaagtcaac acatctgtga actcacagac caagttctta aaccactgtt caaactctgc 420
tacacatcag aatcacctgg agagctttac aaactcccat tgccgagggg cgacgcggcc 480
gcgaatttag tag 493
```

<210> 451

<211> 501

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 451

```
ggcgcgctcc cattcgccat tcaggctgcg caactgttgg gaaggcgcat cggcgcgggc 60
ctcttcgcta ttacgccagc tggcgaaagg gggatgtgct gcaaggcgat taagttgggt 120
aacgccaggg ttttcccagt cncgacgttg taaaacgacg gccagtgaat tgaatttagg 180
tgacnctata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atcctctaga 240
gcggccgcct actactacta aattcgcgcc cgcgctgacg tgggatccnc actgagagag 300
tgagagtgta catgtgctgg acnctgtcca tgaagcactg agcagaagct ggaggcacia 360
cgcncagac actcacagct actcaggagg ctgagaacag gttgaacctg ggaggtggag 420
gttgcaatga gctgagatca ggcnctgcn cccagcatg gatgacagag tgaaactcca 480
tcttaaaaaa aaaaaaaaaa a 501
```

<210> 452

<211> 51

<212> DNA

<213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(51)
 <223> n = A,T,C or G

<400> 452
 agacgggtttc accntttacaa cncctttttag gatgggnntt ggggagcaag c 51

<210> 453
 <211> 317
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(317)
 <223> n = A,T,C or G

<400> 453
 tacatcttgc tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa 60
 acatctgaag agctagtcta tcagcatctg gcaagtgaat tggatgggtc tcagaaccat 120
 ttcacccana cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca 180
 taacaaaccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240
 cccaccaaac tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300
 taccatgtc tttatta 317

<210> 454
 <211> 231
 <212> DNA
 <213> Homo sapiens

<400> 454
 ttcgaggtag aatcaactct cagagtgtag tttccttcta tagatgagtc agcattaata 60
 taagccacgc cagctctctg aaggagtctt gaattctcct ctgctcactc agtagaacca 120
 agaagaccac attcttctgc atcccagctt gcaaacaaaa ttgttcttct aggtctccac 180
 ccttctcttt tcagtgttcc aaagctcctc acaatttcat gaacaacagc t 231

<210> 455
 <211> 231
 <212> DNA
 <213> Homo sapiens

<400> 455
 taccaaagag ggcataataa tcagtctcac agtaggggtc accatcctcc aagtgaaaaa 60
 cattgttccg aatgggcttt ccacaggcta cacacacaaa acaggaaaca tgccaagttt 120
 gtttcaacgc attgatgact tctccaagga tcttcttttg gcacgacca cattcagggg 180
 caaagaattt ctcatagcac agtcacaaat acagggtctc tttctcctct a 231

<210> 456
 <211> 231
 <212> DNA
 <213> Homo sapiens

<400> 456
 ttggcaggta cccttacaaa gaagacacca taccttatgc gttattaggt ggaataatca 60
 ttccattcag tattatcggt attattcttg gagaaacctt gtctgtttac tgtaaccttt 120
 tgcactcaaa ttcctttatc aggaataact acatagccac tatttataaa gccattggaa 180

ccttttttatt tgggtgcagct gctagtcagt ccctgactga cattgccaaag t 231

<210> 457
<211> 231
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(231)
<223> n = A,T,C or G

<400> 457
cgagggtaccc aggggtctga aaatctctnn ttantagtc gatagcaaaa ttgttcatca 60
gcatttcctta atatgatctt gctataatta gatatttctc cattagagtt catacagttt 120
tatttgattt tattagcaat ctctttcaga agacccttga gatcattaag ctttgtatcc 180
agttgtctaa atcgatgcct catttcctct gaggtgtcgc tggcttttgt g 231

<210> 458
<211> 231
<212> DNA
<213> Homo sapiens

<400> 458
aggtcttgggt cccccactt ccaactcccct ctactctctc taggactggg ctgggccaag 60
agaagagggg tggttaggga agccgttgag acctgaagcc ccaccctcta ccttccttca 120
acaccctaac cttgggtaac agcatttgga attatcattt gggatgagta gaatttccaa 180
ggtcctgggt taggcatttt gggggggccag accccaggag aagaagattc t 231

<210> 459
<211> 231
<212> DNA
<213> Homo sapiens

<400> 459
ggtaccgagg ctgctgaca cagagaaacc ccaacgcgag gaaaggaatg gccagccaca 60
ccttcgcgaa acctgtggtg gcccaccagt cctaacggga caggacagag agacagagca 120
gccctgcact gttttccctc caccacagcc atcctgtccc tcattggctc tgtgctttcc 180
actatacaca gtcaccgtcc caatgagaaa caagaaggag caccctccac a 231

<210> 460
<211> 231
<212> DNA
<213> Homo sapiens

<400> 460
gcaggtataa catgctgcaa caacagatgt gactaggaac ggccggtgac atggggaggg 60
cctatcaccc tattcttggg ggtgtcttct tcacagtgat catgaagcct agcagcaaat 120
cccactccc cacacgcaca cggccagcct ggagcccaca gaagggtcct cctgcagcca 180
gtggagcttg gtccagctc cagtccaccc ctaccaggct taaggataga a 231

<210> 461
<211> 231
<212> DNA
<213> Homo sapiens

<400> 461
cgaggtttga gaagctctaa tgtgcagggg agccgagaag caggcggcct agggagggtc 60

gcgtgtgctc cagaagagtg tgtgcatgcc agaggggaaa caggcgctg tgtgtcctgg 120
gtgggggttca gtgaggagtg ggaaattggt tcagcagaac caagccgttg ggtgaataag 180
agggggattc catggcactg atagagccct atagtttcag agctgggaat t 231

<210> 462

<211> 231

<212> DNA

<213> Homo sapiens

<400> 462

aggtaccctc attgtagcca tgggaaaatt gatgttcagt ggggatcagt gaattaaatg 60
gggtcatgca agtataaaaa ttaaaaaaaa aagacttcat gcccaatctc atatgatgtg 120
gaagaactgt tagagagacc aacagggtag tgggttagag atttccagag tcttacattt 180
tctagaggag gtatttaatt tcttctcact catccagtgt tgtatttagg a 231

<210> 463

<211> 231

<212> DNA

<213> Homo sapiens

<400> 463

tactccagcc tgggtgacaga gcgagaccct atcaccgccc cccacccac caaaaaaaaa 60
actgagtaga cagggtgtcct cttggcatgg taagtcttaa gtccctctcc agatctgtga 120
catttgacag gtgtcttttc ctctggacct cgggtgtccc atctgagtga gaaaaggcag 180
tggggagggtg gatcttccag tcgaagcggg atagaagccc gtgtgaaaag c 231

<210> 464

<211> 231

<212> DNA

<213> Homo sapiens

<400> 464

gtactctaag attttatcta agttgccttt tctgggtggg aaagtttaac cttagtgcact 60
aaggacatca catatgaaga atgtttaagt tggagggtggc aacgtgaatt gcaaacaggg 120
cctgtctcag tgactgtgtg cctgtagtcc cagctactcg ggagtctgtg tgaggccagg 180
gggtgccagcg caccagctag atgctctgta acttctaggc cccattttcc c 231

<210> 465

<211> 231

<212> DNA

<213> Homo sapiens

<400> 465

catgttggtg tagctgtggt aatgctggct gcatctcaga cagggttaac ttcagctcct 60
gtggcaaatt agcaacaaat tctgacatca tatattatggt ttctgtatct ttgttgatga 120
aggatggcac aatttttgct tgtgttcata atatactcag attagtctcag ctccatcaga 180
taaactggag acatgcagga cattagggtg gtgtgttagc tctggtaatg a 231

<210> 466

<211> 231

<212> DNA

<213> Homo sapiens

<400> 466

cagggtacctc ttccattgg atactgtgct agcaagcatg ctctccgggg tttttttaat 60
ggccttcgaa cagaacttgc cacataccca ggtataatag tttctaacat ttgccaggga 120
cctgtgcaat caaatattgt ggagaattcc ctagtggag aagtcacaaa gactataggc 180
aataatggag accagtccca caagatgaca accagtcgtt gtgtgcggt g 231

<210> 467
<211> 311
<212> DNA
<213> Homo sapiens

<400> 467
gtacaccctg gcacagtcca atctgaactg gttcggcact catctttcat gagatggatg 60
tggtagcttt tctccttttt catcaagact cctcagcagg gagcccagac cagcctgcac 120
tgtgccttaa cagaaggtct tgagattcta agtgggaatc atttcagtga ctgtcatgtg 180
gcatgggtct ctgcccgaagc tcgtaatgag actatagcaa ggcggctgtg ggacgtcagt 240
tgtgacctgc tgggcctccc aatagactaa caggcagtgc cagttggacc caagagaaga 300
ctgcagcaga c 311

<210> 468
<211> 3112
<212> DNA
<213> Homo sapiens

<400> 468
cattgtgttg ggagaaaaac agaggggaga tttgtgtggc tgcagccgag ggagaccagg 60
aagatctgca tggtagggaag gacctgatga tacagagttt gataggagac aattaaaggc 120
tggaaggcac tggatgcctg atgatgaagt ggactttcaa actggggcac tactgaaacg 180
atgggatggc cagagacaca ggagatgagt tggagcaagc tcaataacaa agtggttcaa 240
cgaggacttg gaattgcatg gagctggagc tgaagtttag cccaattgtt tactagttag 300
gtgaatgtgg atgattggat gatcatttct catctctgag cctcaggttc cccatccata 360
aaatgggata cacagtatga tctataaagt gggatatagt atgactact tcaactggtt 420
atttgaagga tgaattgaga taatttattt cagggtgcct gaacaatgcc cagattagta 480
catttgggtg aactgagaaa tggcataaca ccaaatttaa tatatgtcag atgttactat 540
gattatcatt caatctcata gttttgtcat ggcccaattt atcctcactt gtgcctcaac 600
aaattgaact gtaacaaaag gaatctctgg tcttgggtaa tggctgagca ccactgagca 660
tttccattcc agttggcttc ttgggtttgc tagctgcac actagtcac ttaataaat 720
gaagttttaa catctctcca gtgatttttt tatctcacct ttgaagatac tatgttatgt 780
gattaaataa agaacttgag aagaacaggt ttcattaaac ataaaatcaa tgtagacgca 840
aattttctgg atgggcaata cttatgttca caggaaatgc tttaaaatat gcagaagata 900
attaaatggc aatggacaaa gtgaaaaact tagacttttt tttttttttt ggaagtatct 960
ggatgttcct tagtcactta aaggagaact gaaaaatagc agtgagttcc acataatcca 1020
acctgtgaga ttaaggctct ttgtggggaa ggacaaagat ctgtaaatat acagtttcct 1080
tccaaagcca acgtcgaatt ttgaaacata tcaaagctct tcttcaagac aaataatcta 1140
tagtacatct ttcttatggg atgcacttat gaaaaatggt ggctgtcaac atctagtcac 1200
tttagctctc aaaatgggtc attttaagag aaagttttag aatctcatat ttattcctgt 1260
ggaaggacag cattgtggct tggactttat aaggtcttta ttcaactaaa taggtgagaa 1320
ataagaaagg ctgctgactt taccatctga ggccacacat ctgctgaaat ggagataatt 1380
aacatcacta gaaacagcaa gatgacaata taatgtctaa gtagtgacat gtttttgcac 1440
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<211> 2229

<212> DNA

<213> Homo sapiens

<400> 469

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2229

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<211> 2426

<212> DNA

<213> Homo sapiens

<400> 470

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2426

<210> 471

<211> 812

<212> DNA

<213> Homo sapiens

<400> 471

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812

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<211> 515

<212> DNA

<213> Homo sapiens

<220>

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<400> 472

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<211> 5829

<212> DNA

<213> Homo sapiens

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<211> 1594

<212> DNA

<213> Homo sapiens

<400> 474

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<210> 475

<211> 2414
<212> DNA
<213> Homo sapiens

<220>
<221> unsure
<222> (33)
<223> n=A,T,C or G

<400> 475
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<210> 476
<211> 3434
<212> DNA
<213> Homo sapiens

<400> 476

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```

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His Tyr His Arg Asp Thr Asp Thr Arg Arg His His His Met Asp Thr  
                20                      25                        30  
  
Leu Ser His Tyr His Arg Asp Thr Arg His His Thr Val Thr Trp Thr  
            35                      40                        45  
  
His His His Thr His Glu His Thr Asp Thr Leu Pro Tyr Gly His Trp  
    50                      55                        60  
  
His Thr His Cys His Thr Val Thr Trp Thr His Leu His Thr Ile Thr  
    65                      70                        75                        80  
  
Pro Pro His Thr Leu Pro Val Asp Thr Arg Thr His Arg His Cys His  
                85                      90                        95  
  
Thr Asp Thr Gln Asn Thr Val Thr Arg Arg His His His Ala Asp Thr  
            100                      105                        110  
  
Pro Pro Leu Trp Cys Arg Leu Asn Tyr Pro Ala Gly Gly Thr Ala Val  
    115                      120                        125  
  
Ala Tyr Ser Cys Leu Ser Asp Trp Leu Ser Pro Gln  
    130                      135                        140
```

```

<400> 478
Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
                    5                      10                      15

Ser His Gly His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
                20                      25                      30

Gly Glu Ile Thr Trp Thr His His His Thr Ile Thr Gly Thr Gln Thr
                35                      40                      45

His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
                50                      55                      60

Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
    65                      70                      75                      80

Pro Thr His Cys His Met Asp Thr Gly Thr His Thr Ala Thr Leu Ser
                85                      90                      95

```

His Gly His Thr Ser Thr Pro Ser His His His Thr His Cys Leu Trp
 100 105 110

Thr Gln Gly His Thr Asp Thr Val Thr Gln Ile His Lys Thr Leu Ser
 115 120 125

His Gly Asp Ile Thr Met Gln Ile His His His Ser Gly Ala Val
 130 135 140

<210> 479

<211> 222

<212> PRT

<213> Homo sapiens

<400> 479

Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
 5 10 15

Ser His Glu His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
 20 25 30

Gly Glu Ile Thr Leu Thr His His His Thr Ile Thr Gly Thr Gln Thr
 35 40 45

His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
 50 55 60

Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
 65 70 75 80

Pro Thr His Cys His Met Asp Thr Ala Thr His Thr Ala Thr Leu Ser
 85 90 95

His Gly His Thr Ser Ile Pro Ser His His His Thr His Cys His Val
 100 105 110

Asp Thr Arg Thr His Arg His Cys His Thr Asp Thr Gln Asn Thr Val
 115 120 125

Thr Arg Arg His His His Ala Asp Thr Pro Pro His Gly His Ser Thr
 130 135 140

Arg His Ser Ala Thr Gln Ile His His His Thr Glu Met Arg Thr His
 145 150 155 160

Cys His Thr Asp Thr Thr Thr Ser Leu Pro His Phe His Val Ser Ala
 165 170 175

Gly Gly Val Gly Pro Thr Thr Leu Gly Ser Asn Arg Glu Ile Thr Trp
 180 185 190

Thr Tyr Ser Glu Gly Lys Ile Phe Phe Tyr Phe Leu Gly Asn Gln Ala
 195 200 205

Arg Leu Cys Leu Lys Lys Arg Lys Lys Lys Gln Tyr Thr Val
 210 215 220

<210> 480
 <211> 144
 <212> PRT
 <213> Homo sapiens

<400> 480
 Met Glu Pro Tyr Arg Gly Asn Glu Gln Pro Ser Gln Glu Gln Gly Val
 5 10 15
 Cys Cys Leu Trp Gly Leu Gln Ser Leu Pro Gln Gly Ser Tyr Val Thr
 20 25 30
 Val Gly Phe Leu Val Val Lys Arg Gln Thr Ile Gly Arg Leu Glu Arg
 35 40 45
 Asp Phe Met Phe Lys Cys Arg Lys Gln Pro Gly Leu Pro Pro Ser Gly
 50 55 60
 Leu Cys Leu Leu Trp Pro Trp Pro Asn Leu Glu Phe Gly Arg Arg Gln
 65 70 75 80
 Asp Arg Leu Thr Trp Ser Ser Val Ser Val Ala Gly Val Cys Ala Cys
 85 90 95
 Arg Ala Arg Pro Gly Trp Leu Gly Glu Gln Pro Ala Thr Ser Ala Gly
 100 105 110
 Val Arg Leu Glu Gln Val Glu Gln Pro Pro Ala His Pro Leu Gln Glu
 115 120 125
 Ala Gly Val Ala Arg Phe Pro Arg Pro Glu Trp Val Pro Pro Asn Gly
 130 135 140

<210> 481
 <211> 167
 <212> PRT
 <213> Homo sapiens

<400> 481
 Met His Gly Pro Gln Val Leu Ala Arg Cys Ser Glu Cys Ala Cys Pro
 5 10 15
 Ala Leu Ala Ala Thr Ser Ala Gly Val Arg Leu Glu Gly Val Asp Arg
 20 25 30
 Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys Ser His Ser
 35 40 45
 Leu Ser Gly Cys His Leu Met Ala Asp Gly Ala Lys Ala Leu Gly Lys
 50 55 60
 Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr Asp Val Pro


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<210> 482
<211> 143
<212> PRT
<213> Homo sapiens
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<400> 482  
Met Glu Pro Tyr Arg Gly Asn Lys Lys Gln Val Gln Glu Lys Gly Val  
                    5                      10                      15  
  
Pro Cys Leu Trp Gly Ser Ser Pro Cys Leu Arg Cys His Met Ala Leu  
                20                      25                      30  
  
Arg Ala Ser Trp Leu Pro Gly Gly Gly Pro Gln Ala Ile Leu Gly Arg  
        35                        40                        45  
  
Thr Leu Cys Ser Ser Ala Glu Ser Ser Gln Asp Cys His Pro Gly Gly  
    50                         55                         60  
  
Pro Ser Ile Ala Leu Ala Lys Pro Cys Arg Gly Val Trp Leu Leu Phe  
   65                          70                          75                       80  
  
Glu Pro Ala Trp Pro Pro Trp His Ala Arg Ala Pro Gly Ala Gly Thr  
           85                             90                             95  
  
Leu Leu Arg Val Cys Leu Ser Cys Leu Gly Cys His Leu Cys Gly Gly  
       100                     105                     110  
  
Ala Ser Gly Gly Gly Gly Pro Ala Thr Asn Leu Thr Gln Ser Arg Lys  
      115                           120                           125  
  
Trp Met Ala Met Phe Pro Gln Pro Glu Trp Leu Pro Pro Asp Gly  
    130                   135                   140
```

```
<210> 483
<211> 143
<212> PRT
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<213> Homo sapiens

<400> 483

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Met Glu Thr Gln Arg Gly Asn Lys Gln Arg Ala Gln Glu Gln Gly Val
      5              10              15
Cys Cys Leu Trp Gly Ser Ser Pro Cys Leu Gly Ser Tyr Gly Thr Ala
      20              25              30
Gly Phe Leu Val Ala Lys Arg Arg Thr Thr Gly Leu Leu Glu Glu Asp
      35              40              45
Phe Thr Phe Lys Cys Arg Lys Gln Pro Lys Leu Pro Ser Met Arg Leu
      50              55              60
Ser Leu Leu Trp Pro Trp Arg Asp Leu Lys Phe Val Pro Arg Gln Asp
      65              70              75              80
Lys Leu Thr Arg Ser Ser Val Ser Val Ala Gly Ala Tyr Ala Cys Arg
      85              90              95
Ala Gly Pro Gly Trp Leu Lys Glu Gln Pro Ala Thr Ser Ala Arg Val
      100             105             110
Arg Leu Val Gln Ala Glu His Pro Pro Pro His Pro Leu Glu Glu Val
      115             120             125
Gly Met Ala Arg Phe Pro Gln Pro Glu Cys Leu Pro Pro Tyr Cys
      130             135             140

```

<210> 484

<211> 30

<212> PRT

<213> Homo Sapien

<400> 484

```

Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe
  1      5              10              15
Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile
      20              25              30

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<210> 485

<211> 31

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 485

gggaagctta tcacctatgt gccgcctctg c

<210> 486

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 486

gcgaattctc acgctgagta ttggcc

27

<210> 487

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 487

cccgaattct tagctgccca tccgaacgcc ttcac

36

<210> 488

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 488

gggaagcttc ttccccggct gcaccagctg tgc

33

<210> 489

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 489

Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala
1 5 10 15
Ser Val Ala

<210> 490

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 490

Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys
1 5 10 15
Leu Ser His Ser
20

<210> 491

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 491

Thr	Cys	Leu	Ser	His	Ser	Val	Ala	Val	Val	Thr	Ala	Ser	Ala	Ala	Leu
1				5					10					15	
Thr	Gly	Phe	Thr												
			20												

<210> 492

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 492

Ala	Leu	Thr	Gly	Phe	Thr	Phe	Ser	Ala	Leu	Gln	Ile	Leu	Pro	Tyr	Thr
1				5					10					15	
Leu	Ala	Ser	Leu												
			20												

<210> 493

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 493

Tyr	Thr	Leu	Ala	Ser	Leu	Tyr	His	Arg	Glu	Lys	Gln	Val	Phe	Leu	Pro
1				5					10					15	
Lys	Tyr	Arg	Gly												
			20												

<210> 494

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 494

Leu	Pro	Lys	Tyr	Arg	Gly	Asp	Thr	Gly	Gly	Ala	Ser	Ser	Glu	Asp	Ser
1				5					10					15	
Leu	Met	Ile	Ser												
			20												

<210> 495

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 495

Asp Ser Leu Met Thr Ser Phe Leu Pro Gly Pro Lys Pro Gly Ala Pro
1 5 10 15
Phe Pro Asn Gly
20

<210> 496

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 496

Ala Pro Phe Pro Asn Gly His Val Gly Ala Gly Gly Ser Gly Leu Leu
1 5 10 15
Pro Pro Pro Pro Ala
20

<210> 497

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 497

Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser Ala Cys Asp Val
1 5 10 15
Ser Val Arg Val
20

<210> 498

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 498

Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala Arg Val
1 5 10 15
Val Pro Gly Arg
20

<210> 499

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 499

Arg	Val	Val	Pro	Gly	Arg	Gly	Ile	Cys	Leu	Asp	Leu	Ala	Ile	Leu	Asp
1				5				10						15	
Ser	Ala	Phe	Leu												
				20											

<210> 500

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 500

Leu	Asp	Ser	Ala	Phe	Leu	Leu	Ser	Gln	Val	Ala	Pro	Ser	Leu	Phe	Met
1				5				10						15	
Gly	Ser	Ile	Val												
				20											

<210> 501

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 501

Phe	Met	Gly	Ser	Ile	Val	Gln	Leu	Ser	Gln	Ser	Val	Thr	Ala	Tyr	Met
1				5				10						15	
Val	Ser	Ala	Ala												
				20											

<210> 502

<211> 414

<212> DNA

<213> Homo Sapien

<220>

<221> misc_feature

<222> (1) ... (414)

<223> n = A,T,C or G

<400> 502

caccatggag	acaggcctgc	gctggctttt	cctggctcgt	gtgctcaaag	gtgtccaatg	60
tcagtcggtg	gaggagtccg	ggggtcgcct	ggtcacgcct	gggacacctt	tgacantcac	120
ctgtagagtt	tttggaatng	acctcagtag	caatgcaatg	agctgggtcc	gccaggctcc	180
agggaaaggg	ctggaatgga	tcggagccat	tgataattgt	ccacantacg	cgacctgggc	240
gaaaggccga	ttnatnattt	ccaaaacctn	gaccacggtg	gatttgaaaa	tgaccagtcc	300
gacaaccgag	gacacggcca	cctatTTTTg	tggcagaatg	aatactggta	atagtgggtg	360
gaagaatatt	tggggccag	gcacctgggt	caccgnttcc	tcagggaac	ctaa	414

<210> 503

<211> 379

<212> DNA

<213> Homo Sapiens

<220>

<221> misc_feature

<222> (1)...(379)

<223> n = A,T,C or G

<400> 503

atnogatggt	gcttgggtcaa	aggtgtccag	tgctagtcgg	tggaggagtc	cggggggtcgc	60
ctgggtcacgc	ctgggacacc	cctgacactc	acctgcaccg	tntctggatt	ngacatcagt	120
agctatggag	tgagctgggt	ccgccaggct	ccagggaagg	ggctgggnata	catcggatca	180
ttagtagtag	tggtacattt	tacgcgagct	gggcgaaagg	ccgattcacc	atttccaaaa	240
cctngaccac	ggtggatttg	aaaatcacca	gtttgacaac	cgaggacacg	gccacctatt	300
tntgtgccag	aggggggttt	aattataaag	acatttgggg	cccaggcacc	ctggtcaccg	360
tntccttagg	gcaacctaa					379

<210> 504

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 504

Gly	Phe	Thr	Asn	Tyr	Thr	Asp	Phe	Glu	Asp	Ser	Pro	Tyr	Phe	Lys	Glu
1			5					10						15	
Asn	Ser	Ala													

<210> 505

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 505

Lys	Glu	Asn	Ser	Ala	Phe	Pro	Pro	Phe	Cys	Cys	Asn	Asp	Asn	Val	Thr
1			5					10					15		
Asn	Thr	Ala	Asn												
			20												

<210> 506

<211> 407

<212> DNA

<213> Homo Sapien

<400> 506

atggagacag	gcctgcgtg	gcttctcctg	gtcgtgcgc	tcaaagggtg	ccagtgtcag	60
tcgctggagg	agtcggggg	tcgcctggtc	acgcctggga	caccctgac	actcacctgc	120
accgtctctg	gattctccct	cagtagcaat	gcaatgatct	gggtccgcca	ggctccaggg	180
aaggggctgg	aatacatcgg	atacattagt	tatggtggtg	gcgcatacta	cgcgagctgg	240
gtgaaaggcc	gattcaccat	ctccaaaacc	tcgaccacgg	tggatctgag	aatgaccagt	300
ctgacaaccg	aggacacggc	cacctatttc	tgtgccagaa	atagtgattt	tagtggtatg	360
ttgtggggcc	caggcaccc	ggtcaccgtc	tcctcagggc	aacctaa		407

<210> 507
 <211> 422
 <212> DNA
 <213> Homo Sapien

<400> 507
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 tcggtggagg agtcgggggg tcgcctggtc acgcctggga caccctgac actcacctgt 120
 acagtctctg gattctccct cagcaactac gacctgaact gggtcgcca ggctccaggg 180
 aaggggctgg aatggatcgg gatcattaat tatgttggtg ggacggacta cgcgaactgg 240
 gcaaaaggcc ggttcaccat ctccaaaacc tcgaccaccg tggatctcaa gatcgccagt 300
 ccgacaaccg aggacacggc cacctatttc tgtgccagag ggtggaagtg cgatgagtct 360
 ggtccgtgct tgcgcattct gggcccaggc accctgggtc ccgtctcctt agggcaacct 420
 aa 422

<210> 508
 <211> 411
 <212> DNA
 <213> Homo Sapiens

<220>
 <221> misc_feature
 <222> (1) ... (411)
 <223> n = A,T,C or G

<400> 508
 atggagacag gcctgcgctg cttctcctgg tcgctgtgct caaagggtgc cagtgtcagt 60
 cgggtggagg gtccgggggt cgctgggtca cgctggggac accctgaca ctacacctgca 120
 cagtctctgg aatcgacctc agtagctact gcatgagctg ggtccgccag gctccaggga 180
 aggggctgga atggatcgga atcattggta ctctgggtga cacatactac gcgagggtggg 240
 cgaaaggccg attcaccatc tccaaaacct cgaccacggg gcatntgaaa atcnccagtc 300
 cgacaaccga ggacacggcc acctatttct gtgccagaga tcttcgggat ggtagtagta 360
 ctggttatta taaaatctgg ggcccaggca cctgggtcac cgtctccttg g 411

<210> 509
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 509
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 1 5 10 15

<210> 510
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 510
 Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu Ile
 1 5 10 15

<210> 511
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 511

Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gly Gln Asp Gln Lys
1 5 10 15

<210> 512
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 512

Asp Ser Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu
1 5 10 15

<210> 513
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 513

Ala Pro Cys Gly Gln Val Gly Val Pro Asx Val Tyr Thr Asn Leu
1 5 10 15

<210> 514
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 514

Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
1 5 10 15

<210> 515
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 515
Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg
1 5 10 15

<210> 516
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 516
Val Ser Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln
1 5 10 15

<210> 517
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 517
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met
1 5 10 15

<210> 518
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 518
Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly
1 5 10 15

<210> 519
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 519
Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg Asn Tyr Asp Glu Gly Cys
1 5 10 15
Gly

<210> 520
<211> 25
<212> PRT
<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 520

Val	Gly	Glu	Gly	Leu	Tyr	Gln	Gly	Val	Pro	Arg	Ala	Glu	Pro	Gly	Thr
1				5				10						15	
Glu	Ala	Arg	Arg	His	Tyr	Asp	Glu	Gly							
			20				25								

<210> 521

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 521

Ala	Pro	Phe	Pro	Asn	Gly	His	Val	Gly	Ala	Gly	Gly	Ser	Gly	Leu	Leu
1				5				10						15	
Pro	Pro	Pro	Pro	Ala											
				20											

<210> 522

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 522

Leu	Leu	Val	Val	Pro	Ala	Ile	Lys	Lys	Asp	Tyr	Gly	Ser	Gln	Glu	Asp
1				5				10						15	
Phe	Thr	Gln	Val												
			20												

<210> 523

<211> 254

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<220>

<221> VARIANT

<222> (1)...(254)

<223> Xaa = any amino acid

<400> 523

Met	Ala	Thr	Ala	Gly	Asn	Pro	Trp	Gly	Trp	Phe	Leu	Gly	Tyr	Leu	Ile
1				5				10						15	
Leu	Gly	Val	Ala	Gly	Ser	Leu	Val	Ser	Gly	Ser	Cys	Ser	Gln	Ile	Ile
			20				25				30				
Asn	Gly	Glu	Asp	Cys	Ser	Pro	His	Ser	Gln	Pro	Trp	Gln	Ala	Ala	Leu
		35				40					45				

Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln
 50 55 60
 Trp Val Leu Ser Ala Thr His Cys Phe Gln Asn Ser Tyr Thr Ile Gly
 65 70 75 80
 Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met
 85 90 95
 Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu
 100 105 110
 Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu
 115 120 125
 Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala
 130 135 140
 Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg
 145 150 155 160
 Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu
 165 170 175
 Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys
 180 185 190
 Ala Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser Gly
 195 200 205
 Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly
 210 215 220
 Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu
 225 230 235 240
 Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 245 250

<210> 524
 <211> 765
 <212> DNA
 <213> Homo sapien

<400> 524
 atggccacag caggaaatcc ctggggctgg ttctgggggt acctcatcct tgggtgtcgca 560
 ggatcgctcg tctctggtag ctgcagccaa atcataaacg gcgaggactg cagcccgcac 120
 tcgcagccct ggcaggcggc actgggtcatg gaaaacgaat tgttctgctc gggcgctcctg 180
 gtgcatccgc agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg 240
 ctgggcctgc acagtcttga ggccgaccaa gagccaggga gccagatggt ggaggccagc 300
 ctctccgtac ggcacccaga gtacaacaga cccttgctcg ctaacgacct catgctcatc 360
 aagttggacg aatccgtgtc cgagtctgac accatccgga gcacagcat tgcttcgcag 420
 tgccctaccg cggggaactc ttgcctcgtt tctggctggg gtctgctggc gaacggcaga 480
 atgcctaccg tgetgcagtg cgtgaacgtg tcggtggtgt ctgaggaggt ctgcagtaag 540
 ctctatgacc cgctgtacca cccagcatg ttctgcgccc gcggagggca agaccagaag 600
 gactcctgca acggtgactc tggggggccc ctgatctgca acgggtactt gcagggcctt 660
 gtgtctttcg gaaaagccc gtgtggccaa gttggcgtgc caggtgtcta caccaacctc 720
 tgcaaattca ctgagtggat agagaaaacc gtccaggcca gttaa 765

<210> 525
 <211> 254
 <212> PRT
 <213> Homo sapien

<400> 525
 Met Ala Thr Ala Gly Asn Pro Trp Gly Trp Phe Leu Gly Tyr Leu Ile
 1 5 10 15
 Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile
 20 25 30
 Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu

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<210> 526
<211> 963
<212> DNA
<213> Homo sapiens
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<400>	526						
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aaagcccatt	tctgggttgg	cttccccctc	ctttccatgt	atgtagtggc	aatgtttgga	120	
aactgcatcg	tggctcttcac	cgtaaggacg	gaacgcagcc	tgcacgctcc	gatgtacctc	180	
tttctctgca	tgcttgccagc	cattgacctg	gccttatcca	catccaccat	gcctaagatc	240	
cttgcccctt	tctgggttga	ttcccagagc	attagctttg	aggcctgtct	taccagatg	300	
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caggatgtaa	tgaagttaggc	ctatgcagac	actttgcccc	atgtggtata	tggctcttact	600	
gccattctgc	tggctcatggg	cgtggacgta	atgttcatct	ccttgtccta	ttttctgata	660	
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caccgccttg	gaaacagcct	tcatcccatt	gtgcgtgttg	tcatgggtga	catctacctg	840	
ctgtgcctc	ctgtcatcaa	tcccatcatc	tatgggtgcca	aaaccaaaca	gatcagaaca	900	
cgggtgctgg	ctatgttcaa	gatcagctgt	gacaaggact	tgcaggctgt	gggaggcaag	960	
tga						963	

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<210> 527
<211> 320
<212> PRT
<213> Homo sapiens
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<400> 527

305
310
315
320

<210> 528
<211> 20
<212> DNA
<213> Homo Sapien

<400> 528
actatgggtcc agaggctgtg 20

<210> 529
<211> 20
<212> DNA
<213> Homo Sapien

<400> 529
atcacctatg tgccgcctct 20

<210> 530
<211> 1852
<212> DNA
<213> Homo sapiens

<400> 530
ggcacgagaa ttaaaaccct cagcaaaaaca ggcatagaag ggacatacct taaagtaata 60
aaaaccacct atgacaagcc cacagccaac ataatactaa atgggggaaaa gttagaagca 120
tttcctctga gaactgcaac aataaataca aggatgctgg atttttgtcaa atgccttttc 180
tgtgtctgtt gagatgctta tgtgactttg cttttaattc tgtttatgtg attatcacat 240
ttattgactt gcctgtgtta gaccggaaga gctgggggtgt ttctcaggag ccaccgtgtg 300
ctgcggcagc ttcgggataa cttgaggtcg catcactggg gaagaaacac aytctgttcc 360
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ggagtctctc cttcatagtt catccatag gctccagagg aaaattatat tattttgtta 480
tggatgaaga gtattacgtt gtgcagatat actgcagtgt cttcatctct tgatgtgtga 540
ttgggtaggt tccaccatgt tgccgcagat gacatgattt cagtacctgt gtctggctga 600
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ggatcagcaa gtatagtcag cctctactt gagcaaaatg ttgatgtatc ttctcaagat 1560
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aagacttaaa gctgacatca gaggaagagt cacaaggct taaaggaagt gaaaacagcc 1740
agccagagct agaagattta tggctattga agaagaatga agaacacgga agtactcatg 1800
tgggattccc agaaaacctg actaacggtg ccgctgctgg caatggtgat ga 1852

<210> 531
<211> 879

<212> DNA

<213> Homo sapiens

<400> 531

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atgcatcttt catttccctgc atttcttccct ccctggatgg acaggggggag cggcaagagc 60
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tgcaagtggg gctgccactg cttcccctgc tgcaggggga gcggcaagag caacgtgggc 180
gcttggggag actacgatga cagcgccctc atggatcca ggtaccacgt ccatggagaa 240
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cttaatgtcc ttgacaacaa aaagaggaca gctctgacaa aggccgtaca atgccaggaa 480
gatgaatgtg cgtaaatgtt gctggaacat ggcactgatc caaatattcc agatgagtat 540
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<210> 532

<211> 292

<212> PRT

<213> Homo sapiens

<400> 532

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Met His Leu Ser Phe Pro Ala Phe Leu Pro Pro Trp Met Asp Arg Gly
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Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp His Asn Asp Ser Ser
      20              25              30
Val Lys Thr Leu Gly Ser Lys Arg Cys Lys Trp Cys Cys His Cys Phe
      35              40              45
Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val Val Ala Trp Gly Asp
      50              55              60
Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr His Val His Gly Glu
      65              70              75              80
Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg
      85              90              95
Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Arg Asp
      100             105             110
Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser
      115             120             125
Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys Gln Leu Asn Val Leu
      130             135             140
Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala Val Gln Cys Gln Glu
      145             150             155             160
Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile
      165             170             175

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Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Val Tyr Asn Glu
 180 185 190

Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu
 195 200 205

Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Ile His Glu
 210 215 220

Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu
 225 230 235 240

Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys
 245 250 255

Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu Glu Gln Asn Val Asp
 260 265 270

Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu Ser Met Leu Phe Leu
 275 280 285

Val Ile Ile Met
 290

<210> 533
 <211> 801
 <212> DNA
 <213> Homo sapiens

<400> 533
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 tatgccactg cagcattctt ggttgccaag aggccaaacca caggccatct tgagaaggag 180
 tttatgttcc actgcagaaa gcagccagga tcaccatcca ggggacttgg tcttctgttg 240
 ccctggccag acatagaatt tgtgccaagg caggacaagc tcactcagag cagcgtgtta 300
 gtacctcaaa tctgtgcgtg ccagacaagg ccaaactggc tcaatgagca accagccacc 360
 tctgcagggg tgcgtctgga ggaggtggac cagccaccaa ccttaccag tcaaggaagt 420
 ggatggccat gttccacag cctgagtggc tgccacctga tggtgatata agcaaaggcc 480
 ttaggaaaag cagatggccc ttggccctac ctttttggtta gaagaactga tgttccatgt 540
 cctgcagcga gtgaggttg tggctgtgcc cccagctcct ggcacaccct cgcagaggtg 600
 actggttgct ctttgagccc tcttagcctt gccagcatg cacaagcctc agtgctacta 660
 ctgtgtaca aatggagcca tataggggaa acgagcagcc atctcaggag caaggtgtat 720
 gctgcctttg ggggctccag tccttgctc aagggtctta tgtcactgtg ggcttcttgg 780
 ttgccaagag gcagaccata g 801

<210> 534
 <211> 266
 <212> PRT
 <213> Homo sapiens

<400> 534
 Met Tyr Lys Leu Gln Cys Asn Asn Cys Ala Thr Asn Gly Ala Thr Glu
 5 10 15

Arg Lys Gln Ala Ala Gly Ser Gly Ala Gly Tyr Ala Leu Pro Ser Ala
 20 25 30

Leu Gln Ser Met Pro Gln Gly Ser Tyr Ala Thr Ala Arg Phe Leu Val
 35 40 45
 Ala Lys Arg Pro Thr Thr Gly His Leu Glu Lys Glu Phe Met Phe His
 50 55 60
 Cys Arg Lys Gln Pro Gly Ser Pro Ser Arg Gly Leu Gly Leu Leu Trp
 65 70 75 80
 Pro Trp Pro Asp Ile Glu Phe Val Pro Arg Gln Asp Lys Leu Thr Gln
 85 90 95
 Ser Ser Val Leu Val Pro Gln Ile Cys Ala Cys Gln Thr Arg Pro Asn
 100 105 110
 Trp Leu Asn Glu Gln Pro Ala Thr Ser Ala Gly Val Arg Leu Glu Glu
 115 120 125
 Val Asp Gln Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys
 130 135 140
 Ser His Ser Leu Ser Gly Cys His Leu Met Ala Asp Ile Ala Lys Ala
 145 150 155 160
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Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr Val Leu Thr Phe Cys	130	135	140
Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr Phe Tyr His Val Gln	145	150	155
Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys His Met Ile Tyr Arg	165	170	175
Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly Lys Thr Thr Thr Gly	180	185	190
Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn Lys Phe Asp Gln Val	195	200	205
Thr Val Phe Leu His Phe Leu Trp Ala Gly Pro Leu Gln Ala Ile Ala	210	215	220
Val Thr Ala Leu Leu Trp Met Glu Ile Gly Ile Ser Cys Leu Ala Gly	225	230	235
Met Ala Val Leu Ile Ile Leu Leu Pro Leu Gln Ser Cys Phe Gly Lys	245	250	255
Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr Phe Thr Asp Ala Arg	260	265	270
Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile Arg Ile Ile Lys Met	275	280	285
Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile Thr Asn Leu Arg Lys	290	295	300
Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys Leu Arg Gly Met Asn	305	310	315
Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile Val Phe Val Thr Phe	325	330	335
Thr Thr Tyr Val Leu Leu Gly Ser Val Ile Thr Ala Ser Arg Val Phe	340	345	350
Val Ala Val Thr Leu Tyr Gly Ala Val Arg Leu Thr Val Thr Leu Phe	355	360	365
Phe Pro Ser Ala Ile Glu Arg Val Ser Glu Ala Ile Val Ser Ile Arg	370	375	380

Arg Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile Ser Gln Arg Asn Arg
 385 390 395 400
 Gln Leu Pro Ser Asp Gly Lys Lys Met Val His Val Gln Asp Phe Thr
 405 410 415
 Ala Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr Leu Gln Gly Leu Ser
 420 425 430
 Phe Thr Val Arg Pro Gly Glu Leu Leu Ala Val Val Gly Pro Val Gly
 435 440 445
 Ala Gly Lys Ser Ser Leu Leu Ser Ala Val Leu Gly Glu Leu Ala Pro
 450 455 460
 Ser His Gly Leu Val Ser Val His Gly Arg Ile Ala Tyr Val Ser Gln
 465 470 475 480
 Gln Pro Trp Val Phe Ser Gly Thr Leu Arg Ser Asn Ile Leu Phe Gly
 485 490 495
 Lys Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val Ile Lys Ala Cys Ala
 500 505 510
 Leu Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly Asp Leu Thr Val Ile
 515 520 525
 Gly Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln Lys Ala Arg Val Asn
 530 535 540
 Leu Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile Tyr Leu Leu Asp Asp
 545 550 555 560
 Pro Leu Ser Ala Val Asp Ala Glu Val Ser Arg His Leu Phe Glu Leu
 565 570 575
 Cys Ile Cys Gln Ile Leu His Glu Lys Ile Thr Ile Leu Val Thr His
 580 585 590
 Gln Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile Leu Ile Leu Lys Asp
 595 600 605
 Gly Lys Met Val Gln Lys Gly Thr Tyr Thr Glu Phe Leu Lys Ser Gly
 610 615 620
 Ile Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn Glu Glu Ser Glu Gln
 625 630 635 640
 Pro Pro Val Pro Gly Thr Pro Thr Leu Arg Asn Arg Thr Phe Ser Glu
 645 650 655
 Ser Ser Val Trp Ser Gln Gln Ser Ser Arg Pro Ser Leu Lys Asp Gly
 660 665 670
 Ala Leu Glu Ser Gln Asp Thr Glu Asn Val Pro Val Thr Leu Ser Glu
 675 680 685

Glu Asn Arg Ser Glu Gly Lys Val Gly Phe Gln Ala Tyr Lys Asn Tyr
 690 695 700
 Phe Arg Ala Gly Ala His Trp Ile Val Phe Ile Phe Leu Ile Leu Leu
 705 710 715 720
 Asn Thr Ala Ala Gln Val Ala Tyr Val Leu Gln Asp Trp Trp Leu Ser
 725 730 735
 Tyr Trp Ala Asn Lys Gln Ser Met Leu Asn Val Thr Val Asn Gly Gly
 740 745 750
 Gly Asn Val Thr Glu Lys Leu Asp Leu Asn Trp Tyr Leu Gly Ile Tyr
 755 760 765
 Ser Gly Leu Thr Val Ala Thr Val Leu Phe Gly Ile Ala Arg Ser Leu
 770 775 780
 Leu Val Phe Tyr Val Leu Val Asn Ser Ser Gln Thr Leu His Asn Lys
 785 790 795 800
 Met Phe Glu Ser Ile Leu Lys Ala Pro Val Leu Phe Phe Asp Arg Asn
 805 810 815
 Pro Ile Gly Arg Ile Leu Asn Arg Phe Ser Lys Asp Ile Gly His Leu
 820 825 830
 Asp Asp Leu Leu Pro Leu Thr Phe Leu Asp Phe Ile Gln Thr Leu Leu
 835 840 845
 Gln Val Val Gly Val Val Ser Val Ala Val Ala Val Ile Pro Trp Ile
 850 855 860
 Ala Ile Pro Leu Val Pro Leu Gly Ile Ile Phe Ile Phe Leu Arg Arg
 865 870 875 880
 Tyr Phe Leu Glu Thr Ser Arg Asp Val Lys Arg Leu Glu Ser Thr Thr
 885 890 895
 Arg Ser Pro Val Phe Ser His Leu Ser Ser Ser Leu Gln Gly Leu Trp
 900 905 910
 Thr Ile Arg Ala Tyr Lys Ala Glu Glu Arg Cys Gln Glu Leu Phe Asp
 915 920 925
 Ala His Gln Asp Leu His Ser Glu Ala Trp Phe Leu Phe Leu Thr Thr
 930 935 940
 Ser Arg Trp Phe Ala Val Arg Leu Asp Ala Ile Cys Ala Met Phe Val
 945 950 955 960
 Ile Ile Val Ala Phe Gly Ser Leu Ile Leu Ala Lys Thr Leu Asp Ala
 965 970 975
 Gly Gln Val Gly Leu Ala Leu Ser Tyr Ala Leu Thr Leu Met Gly Met
 980 985 990
 Phe Gln Trp Cys Val Arg Gln Ser Ala Glu Val Glu Asn Met Met Ile

995 1000 1005
 Ser Val Glu Arg Val Ile Glu Tyr Thr Asp Leu Glu Lys Glu Ala Pro
 1010 1015 1020
 Trp Glu Tyr Gln Lys Arg Pro Pro Pro Ala Trp Pro His Glu Gly Val
 1025 1030 1035 1040
 Ile Ile Phe Asp Asn Val Asn Phe Met Tyr Ser Pro Gly Gly Pro Leu
 1045 1050 1055
 Val Leu Lys His Leu Thr Ala Leu Ile Lys Ser Gln Glu Lys Val Gly
 1060 1065 1070
 Ile Val Gly Arg Thr Gly Ala Gly Lys Ser Ser Leu Ile Ser Ala Leu
 1075 1080 1085
 Phe Arg Leu Ser Glu Pro Glu Gly Lys Ile Trp Ile Asp Lys Ile Leu
 1090 1095 1100
 Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys Lys Met Ser Ile Ile
 1105 1110 1115 1120
 Pro Gln Glu Pro Val Leu Phe Thr Gly Thr Met Arg Lys Asn Leu Asp
 1125 1130 1135
 Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp Asn Ala Leu Gln Glu
 1140 1145 1150
 Val Gln Leu Lys Glu Thr Ile Glu Asp Leu Pro Gly Lys Met Asp Thr
 1155 1160 1165
 Glu Leu Ala Glu Ser Gly Ser Asn Phe Ser Val Gly Gln Arg Gln Leu
 1170 1175 1180
 Val Cys Leu Ala Arg Ala Ile Leu Arg Lys Asn Gln Ile Leu Ile Ile
 1185 1190 1195 1200
 Asp Glu Ala Thr Ala Asn Val Asp Pro Arg Thr Asp Glu Leu Ile Gln
 1205 1210 1215
 Lys Lys Ser Gly Arg Asn Leu Pro Thr Ala Pro Cys
 1220 1225

 <210> 538
 <211> 1261
 <212> PRT
 <213> Homo sapiens

 <400> 538
 Met Tyr Ser Val Leu Pro Glu Asp Arg Ser Gln His Leu Gly Glu Glu
 5 10 15
 Leu Gln Gly Phe Trp Asp Lys Glu Val Leu Arg Ala Glu Asn Asp Ala
 20 25 30
 Gln Lys Pro Ser Leu Thr Arg Ala Ile Ile Lys Cys Tyr Trp Lys Ser
 35 40 45

Tyr Leu Val Leu Gly Ile Phe Thr Leu Ile Glu Glu Ser Ala Lys Val
 50 55 60
 Ile Gln Pro Ile Phe Leu Gly Lys Ile Ile Asn Tyr Phe Glu Asn Tyr
 65 70 75 80
 Asp Pro Met Asp Ser Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr
 85 90 95
 Val Leu Thr Phe Cys Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr
 100 105 110
 Phe Tyr His Val Gln Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys
 115 120 125
 His Met Ile Tyr Arg Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly
 130 135 140
 Lys Thr Thr Thr Gly Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn
 145 150 155 160
 Lys Phe Asp Gln Val Thr Val Phe Leu His Phe Leu Trp Ala Gly Pro
 165 170 175
 Leu Gln Ala Ile Ala Val Thr Ala Leu Leu Trp Met Glu Ile Gly Ile
 180 185 190
 Ser Cys Leu Ala Gly Met Ala Val Leu Ile Ile Leu Leu Pro Leu Gln
 195 200 205
 Ser Cys Phe Gly Lys Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr
 210 215 220
 Phe Thr Asp Ala Arg Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile
 225 230 235 240
 Arg Ile Ile Lys Met Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile
 245 250 255
 Thr Asn Leu Arg Lys Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys
 260 265 270
 Leu Arg Gly Met Asn Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile
 275 280 285
 Val Phe Val Thr Phe Thr Thr Tyr Val Leu Leu Gly Ser Val Ile Thr
 290 295 300
 Ala Ser Arg Val Phe Val Ala Val Thr Leu Tyr Gly Ala Val Arg Leu
 305 310 315 320
 Thr Val Thr Leu Phe Phe Pro Ser Ala Ile Glu Arg Val Ser Glu Ala
 325 330 335
 Ile Val Ser Ile Arg Arg Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile
 340 345 350

Ser Gln Arg Asn Arg Gln Leu Pro Ser Asp Gly Lys Lys Met Val His
 355 360 365
 Val Gln Asp Phe Thr Ala Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr
 370 375 380
 Leu Gln Gly Leu Ser Phe Thr Val Arg Pro Gly Glu Leu Leu Ala Val
 385 390 395 400
 Val Gly Pro Val Gly Ala Gly Lys Ser Ser Leu Leu Ser Ala Val Leu
 405 410 415
 Gly Glu Leu Ala Pro Ser His Gly Leu Val Ser Val His Gly Arg Ile
 420 425 430
 Ala Tyr Val Ser Gln Gln Pro Trp Val Phe Ser Gly Thr Leu Arg Ser
 435 440 445
 Asn Ile Leu Phe Gly Lys Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val
 450 455 460
 Ile Lys Ala Cys Ala Leu Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly
 465 470 475 480
 Asp Leu Thr Val Ile Gly Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln
 485 490 495
 Lys Ala Arg Val Asn Leu Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile
 500 505 510
 Tyr Leu Leu Asp Asp Pro Leu Ser Ala Val Asp Ala Glu Val Ser Arg
 515 520 525
 His Leu Phe Glu Leu Cys Ile Cys Gln Ile Leu His Glu Lys Ile Thr
 530 535 540
 Ile Leu Val Thr His Gln Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile
 545 550 555 560
 Leu Ile Leu Lys Asp Gly Lys Met Val Gln Lys Gly Thr Tyr Thr Glu
 565 570 575
 Phe Leu Lys Ser Gly Ile Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn
 580 585 590
 Glu Glu Ser Glu Gln Pro Pro Val Pro Gly Thr Pro Thr Leu Arg Asn
 595 600 605
 Arg Thr Phe Ser Glu Ser Ser Val Trp Ser Gln Gln Ser Ser Arg Pro
 610 615 620
 Ser Leu Lys Asp Gly Ala Leu Glu Ser Gln Asp Thr Glu Asn Val Pro
 625 630 635 640
 Val Thr Leu Ser Glu Glu Asn Arg Ser Glu Gly Lys Val Gly Phe Gln
 645 650 655
 Ala Tyr Lys Asn Tyr Phe Arg Ala Gly Ala His Trp Ile Val Phe Ile

660					665					670						
Phe	Leu	Ile	Leu	Leu	Asn	Thr	Ala	Ala	Gln	Val	Ala	Tyr	Val	Leu	Gln	
675					680					685						
Asp	Trp	Trp	Leu	Ser	Tyr	Trp	Ala	Asn	Lys	Gln	Ser	Met	Leu	Asn	Val	
690					695					700						
Thr	Val	Asn	Gly	Gly	Gly	Asn	Val	Thr	Glu	Lys	Leu	Asp	Leu	Asn	Trp	
705					710					715					720	
Tyr	Leu	Gly	Ile	Tyr	Ser	Gly	Leu	Thr	Val	Ala	Thr	Val	Leu	Phe	Gly	
725					730					735						
Ile	Ala	Arg	Ser	Leu	Leu	Val	Phe	Tyr	Val	Leu	Val	Asn	Ser	Ser	Gln	
740					745					750						
Thr	Leu	His	Asn	Lys	Met	Phe	Glu	Ser	Ile	Leu	Lys	Ala	Pro	Val	Leu	
755					760					765						
Phe	Phe	Asp	Arg	Asn	Pro	Ile	Gly	Arg	Ile	Leu	Asn	Arg	Phe	Ser	Lys	
770					775					780						
Asp	Ile	Gly	His	Leu	Asp	Asp	Leu	Leu	Pro	Leu	Thr	Phe	Leu	Asp	Phe	
785					790					795					800	
Ile	Gln	Thr	Leu	Leu	Gln	Val	Val	Gly	Val	Val	Ser	Val	Ala	Val	Ala	
805					810					815						
Val	Ile	Pro	Trp	Ile	Ala	Ile	Pro	Leu	Val	Pro	Leu	Gly	Ile	Ile	Phe	
820					825					830						
Ile	Phe	Leu	Arg	Arg	Tyr	Phe	Leu	Glu	Thr	Ser	Arg	Asp	Val	Lys	Arg	
835					840					845						
Leu	Glu	Ser	Thr	Thr	Arg	Ser	Pro	Val	Phe	Ser	His	Leu	Ser	Ser	Ser	
850					855					860						
Leu	Gln	Gly	Leu	Trp	Thr	Ile	Arg	Ala	Tyr	Lys	Ala	Glu	Glu	Arg	Cys	
865					870					875					880	
Gln	Glu	Leu	Phe	Asp	Ala	His	Gln	Asp	Leu	His	Ser	Glu	Ala	Trp	Phe	
885					890					895						
Leu	Phe	Leu	Thr	Thr	Ser	Arg	Trp	Phe	Ala	Val	Arg	Leu	Asp	Ala	Ile	
900					905					910						
Cys	Ala	Met	Phe	Val	Ile	Ile	Val	Ala	Phe	Gly	Ser	Leu	Ile	Leu	Ala	
915					920					925						
Lys	Thr	Leu	Asp	Ala	Gly	Gln	Val	Gly	Leu	Ala	Leu	Ser	Tyr	Ala	Leu	
930					935					940						
Thr	Leu	Met	Gly	Met	Phe	Gln	Trp	Cys	Val	Arg	Gln	Ser	Ala	Glu	Val	
945					950					955					960	
Glu	Asn	Met	Met	Ile	Ser	Val	Glu	Arg	Val	Ile	Glu	Tyr	Thr	Asp	Leu	
965					970					975						

Glu Lys Glu Ala Pro Trp Glu Tyr Gln Lys Arg Pro Pro Pro Ala Trp
 980 985 990
 Pro His Glu Gly Val Ile Ile Phe Asp Asn Val Asn Phe Met Tyr Ser
 995 1000 1005
 Pro Gly Gly Pro Leu Val Leu Lys His Leu Thr Ala Leu Ile Lys Ser
 1010 1015 1020
 Gln Glu Lys Val Gly Ile Val Gly Arg Thr Gly Ala Gly Lys Ser Ser
 1025 1030 1035 1040
 Leu Ile Ser Ala Leu Phe Arg Leu Ser Glu Pro Glu Gly Lys Ile Trp
 1045 1050 1055
 Ile Asp Lys Ile Leu Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys
 1060 1065 1070
 Lys Met Ser Ile Ile Pro Gln Glu Pro Val Leu Phe Thr Gly Thr Met
 1075 1080 1085
 Arg Lys Asn Leu Asp Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp
 1090 1095 1100
 Asn Ala Leu Gln Glu Val Gln Leu Lys Glu Thr Ile Glu Asp Leu Pro
 1105 1110 1115 1120
 Gly Lys Met Asp Thr Glu Leu Ala Glu Ser Gly Ser Asn Phe Ser Val
 1125 1130 1135
 Gly Gln Arg Gln Leu Val Cys Leu Ala Arg Ala Ile Leu Arg Lys Asn
 1140 1145 1150
 Gln Ile Leu Ile Ile Asp Glu Ala Thr Ala Asn Val Asp Pro Arg Thr
 1155 1160 1165
 Asp Glu Leu Ile Gln Lys Lys Ile Arg Glu Lys Phe Ala His Cys Thr
 1170 1175 1180
 Val Leu Thr Ile Ala His Arg Leu Asn Thr Ile Ile Asp Ser Asp Lys
 1185 1190 1195 1200
 Ile Met Val Leu Asp Ser Gly Arg Leu Lys Glu Tyr Asp Glu Pro Tyr
 1205 1210 1215
 Val Leu Leu Gln Asn Lys Glu Ser Leu Phe Tyr Lys Met Val Gln Gln
 1220 1225 1230
 Leu Gly Lys Ala Glu Ala Ala Ala Leu Thr Glu Thr Ala Lys Gln Arg
 1235 1240 1245
 Trp Gly Phe Thr Met Leu Ala Arg Leu Val Ser Asn Ser
 1250 1255 1260

<210> 539

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 539

Cys Leu Ser His Ser Val Ala Val Val Thr

1 5 10

<210> 540

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 540

Ala Val Val Thr Ala Ser Ala Ala Leu

1 5

<210> 541

<211> 14

<212> PRT

<213> Homo sapiens

<400> 541

Leu Ala Gly Leu Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu

5 10

<210> 542

<211> 15

<212> PRT

<213> Homo sapiens

<400> 542

Thr Gln Val Val Phe Asp Lys Ser Asp Leu Ala Lys Tyr Ser Ala

5 10 15

<210> 543

<211> 12

<212> PRT

<213> Homo sapiens

<400> 543

Phe Met Gly Ser Ile Val Gln Leu Ser Gln Ser Val

5 10

<210> 544

<211> 18

<212> PRT

<213> Homo sapiens

<400> 544

Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val Glu Glu Lys Phe

<210> 545

<211> 18

<212> PRT

<213> Homo sapiens

<400> 545

Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala
5 10 15

Ser Val

<210> 546

<211> 29

<212> PRT

<213> Homo sapiens

<400> 546

Phe Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly
5 10 15

Thr Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg Met
20 25

<210> 547

<211> 58

<212> PRT

<213> Homo sapiens

<400> 547

Val Ala Glu Glu Ala Ala Leu Gly Pro Thr Glu Pro Ala Glu Gly Leu
5 10 15

Ser Ala Pro Ser Leu Ser Pro His Cys Cys Pro Cys Arg Ala Arg Leu
20 25 30

Ala Phe Arg Asn Leu Gly Ala Leu Leu Pro Arg Leu His Gln Leu Cys
35 40 45

Cys Arg Met Pro Arg Thr Leu Arg Arg Leu
50 55

<210> 548

<211> 18

<212> PRT

<213> Homo sapiens

<400> 548

Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu

200

5

10

15

Glu Cys

<210> 549

<211> 18

<212> PRT

<213> Homo sapiens

<400> 549

Leu Glu Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg
5 10 15

Gln Ala

<210> 550

<211> 14

<212> PRT

<213> Homo sapiens

<400> 550

Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Arg Pro Phe
5 10

<210> 551

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 551

Phe Asp Lys Ser Asp Leu Ala Lys Tyr Ser Ala
1 5 10

